THE

AMERICAN REVIEW OF TUBERCULOSIS

ABSTRACTS OF TUBERCULOSIS

VOLUME XIV OCTOBER, 1926 ABST. NO. 4

Absorption and Elimination of Volatile Substances.—The fact that the substances used as anesthetics are volatile enables them to be absorbed extremely rapidly up to the high concentration in the blood necessary for an anesthetic action upon the nervous system. Their volatility also allows a more rapid elimination than is possible for any nonvolatile substance. Volatility, or the property of forming a gas or vapor, renders a substance capable of entering or leaving the body through the lungs. The laws governing such absorption and elimination of gases are outlined. To the physician the irritant gases and carbon-monoxide asphyxia are of the greatest interest. With regard to the irritant vapor, the more soluble the gas the more it attacks the upper respiratory tract; the less soluble it is, the more likely it is to act chiefly on the deeper parts, the bronchi and the lungs. For example, ammonia, when inhaled, is largely absorbed on the damp walls of the nares, pharynx, larynx and trachea, cough is excited and the lungs are thus protected. In phosgene poisoning, on the other hand, the chief action is on the lungs themselves. The chief sources of carbon-monoxide poisoning are illuminating gas and automobile exhausts. In treating carbon-monoxide asphyxia it is of greatest importance that carbon dioxide should be administered with the oxygen. Until a sufficient amount of carbon dioxide is reaccumulated in the blood and tissues, efficient breathing does not return, and the injurious conditions within the cells of the nervous system and heart are thus continued long after the body is surrounded by pure air. Evidently the abbreviation of the post-gassing period of depressed breathing and its continued asphyxia are of critical importance in preventing permanent damage. The mixture generally employed is 5 per cent carbon dioxide and 95 per cent oxygen. The aim is to stimulate the breathing of the patient, and to maintain it for an hour or more at such a large volume as will ventilate the poison out of the blood by way of the lungs, and thus clear the body and especially the brain. Oxygen does not stimulate respiration; carbon dioxide does.—*The Absorption and Elimination of Volatile Substances through the Lungs: Anaesthesia, Poisoning by Gases and Vapours in Industry, Treatment of Asphyxia, Y. Henderson, Brit. M. J., January 9, 1926, no. 3393, 41.*—*(J. S. W.)*

Lipodieresis in Lung.—The functions of the lungs as regards gas exchange have been extensively studied. The lung, however, possesses, like the liver, internal organic functions less known. Embryologically, it is derived from the epithelium of the ventral aspect of the foregut and possesses histologically, besides the respiratory epithelium, collections of nucleated cells, rich in lipoids and possessing characters suggesting glandular cells. It is well known that absorbed fats are carried through the thoracic duct to debouche into the left subclavian vein and thence into the right heart and pulmonary circulation. Histological study of dogs' lungs has shown the presence of large fatty particles in the interior of the capillaries. Roger and Binet first studied quantitatively the fat content of venous and arterial blood of dogs after a meal rich in fat. There was a distinct difference in favor of the venous blood. The questions then arose: *1:* What sort of fats are arrested by the lung? *2:* What becomes of the fats which pass through the barrier? Lipodieresis is also distinguished from lipolytic action, the former being a much more complete tranformation. It can best be put in evidence by increasing lipemia, for which purpose 15 cc. of olive oil was injected into the saphenous vein of a dog of 20 kgm. weight. Fragments of lung tissue were removed before injection, and at various

intervals thereafter. By this means 100 gm. of lung tissue were found to retain 7.91 gm. olive oil, which practically all disappeared in forty-eight hours, and 81.7 per cent did so in three hours. One might suppose this to be a transient mechanical retention, the fat being gradually washed out by the circulation and other organs, but further experiments show evidence of intrapulmonary oxidation. In these, individual bronchial trunks were ligated. In sections supplied by these, that is, whose air supply was impeded, the fat content remained much higher. Thus it is concluded that the lung fixes more or less completely the fats brought by the circulation; that the larger the quantity the more energetic its destructive action, for which oxygen is indispensable. Microscopic examination has been made of fragments of lung removed from the injected dogs. The fat is entirely arrested in the alveolar capillaries, obstructing more or less completely their lumina. Serial sections show that the fat globules are rapidly attacked; lacunae appear in their midst and the color reactions change. The oil, however, does not disappear if the tissues are kept in the incubator without ventilation, nor in the lobes of the lungs whose bronchi are shut off. It tends to persist in small congested areas, where, however, endothelial phagocytes attack it. Lipodieresis also occurs in the pleura and air-passages, and also in the blood itself, that is, in the arterial blood. Samples of arterial and venous blood are readily studied after preservation by addition of sodium fluoride, which is both antiseptic and anticoagulant. In 18 hours there was found a diminution of fat content by 35 per cent in the arterial and 3 per cent in the venous blood. If both are well mixed with air the arterial blood shows a loss of 72 per cent fat, the venous 16 per cent. Thus it appears that in traversing the lung the blood acquires the power to destroy fats. This cannot be due purely to oxygenation, as even in venous blood well mixed with oxygen the diminution in fat-content is less than in arterial blood which has passed through the lung. It is concluded that the lung gives up to the blood a ferment which acts on the fats. Further analysis and experiments were done to determine in what group to put fats extracted from the lungs. They were found to be rich in vitamine-A, as determined by their influence on the growth of rats, and to contain also some antirachitic substances, due to specific vitamines and not to their phosphorus content. *Action of the lung on other organic products:* Long ago Chauveau showed that the venous blood is poorer in sugar than the arterial blood. Since then various experimenters have studied the effect of the lung on blood-sugar. It appears that the blood of the left heart contains less glucoprotein than that of the right; this seems to indicate that the lung splits the glucoprotein, and sets the glucose free. If, then, the arterial blood does not constantly contain more glucose than the venous blood, a new factor, glycolysis, must intervene. It was sought to determine whether this splitting of glucoprotein was due to simple oxidation or to a specific action of the lung. Some of the blood from the right heart of an anesthetized dog was sidetracked through a current of oxygen. Some splitting of glucoprotein occurred, but less than in that passing through the lung. It has also been shown (Bert and Scott, Mauriac and Servantie) that the intravenous injection of 0.02 gm. lung extract per kg. lowers the blood sugar slightly, about 10 per cent, thus resembling faintly the effect of insulin. *Summary:* The facts gathered indicate that the lung is not merely a membrane for filtering gases but has internal secretory functions. Its action on fats is most striking, destroying them by a true intravascular digestion, in which oxidation plays an important rôle. This combustion must result in heat production. The lung also acts on carbohydrates, alkaloids, and diverse toxic substances.—*Recherches sur la physiologie du poumon, G. H. Roger and L. Binet, Rev. d. Méd., 1925, i, 1.*—(*A. P.*)

Changes in Liver in Tuberculosis Elsewhere.—The livers from 50 cases of pulmonary and bone and joint tuberculosis were examined histologically, and 450 additional protocols analyzed. The ages varied from 15 to 58 years. Specific changes were found macroscopically in 42 cases (10 per cent). The nodules occurred mostly on the surface of the liver, more rarely in the depth. Their size varied from that of the point of a needle to that of a hemp-seed. Microscopic nodules were present in 43 of the 50 cases (86 per cent), usually occurring in the periphery of the lobules at Glisson's capsule, or more rarely in the lobular tissue. Most of the nodules were round; more rarely diffuse infiltrations of Glisson's capsule or the parenchyma, with atrophy of the neighboring cells. The age of the tubercles was not definitely determinable, but 13 of the 43 presented the older type of tubercles. It is concluded that the tubercles develop during the course of tuberculosis, and not only shortly before death. A hematogenous origin is indicated, since changes in the neighboring organs were not frequent enough to account for any other source. Staining of the tubercle bacilli resulted positively in only 8 of the cases, and in 5 of these the

bacilli were sparse. The livers were grouped into the five following classes: (1) nutmeg liver, or simple venous hyperemia; (2) fatty infiltration, (3) brown and simple atrophy, (4) parenchymatous changes, and (5) amyloid. In most cases the weight and size of the liver were within normal limits or slightly less.—*Zur Frage der Veränderungen der Leber während der Periode der isolierten Phthise, W. J. Schlapobersky, Ztschr. f. Tuberk., 1925, xlii, 473.*—(*H. J. C.*)

Fatty Liver of Phthisis.—There was found a certain relationship between the fatty liver occurring in pulmonary tuberculosis and a diminution of lipolytic action, which stands in distinction to the theory of inhibition of oxidation as a case of the fatty liver.—*Ist die Fettleber bei Lungenschwindsucht ein Ferment-problem? K. W. Clauberg, Virchow's Arch. f. path. Anat., 1924, ccliii, 452.*—(*H. J. C.*)

Chemical Study of Bile and Liver in Tuberculosis.—Struck by the frequency of fatty degeneration of the liver at autopsy of the tuberculous, Monceaux started to work on the chemicopathological problems involved. Both the liver and the gallbladder were studied, the latter being removed after ligation of its duct, and its contents examined twenty-four hours later in the laboratory. The total nitrogen content of the bile was estimated by the Kjeldahl method on the residue after desiccation, and the fatty matter was extracted by chloroform and heat. It is well known that the constitution of the bile undergoes changes in the course of various affections, such as typhus fever, cholera, uremia, etc. In these tuberculous subjects its reaction was most often neutral or slightly acid, its nitrogenous content low, and its urea approaching about that of the blood. The fats, on the other hand, are greatly increased. This must be due either to fatty degeneration of the hepatic tissues or to inability of the tubercle bacilli to transform fatty acids brought from the intestine. The latter explanation is favored. The human liver normally contains from 1.8 to 3.6 per cent fat, a mixture of olein, stearin and palmitin. When excessive fat is ingested this increases, as it does also in the course of certain infections and intoxications, notably poisoning by phosphorous, arsenic and antimony. In these studies the liver was weighed, sectioned and triturated, and heated to not over 60°C. In very fat livers a pale yellow oil might be seen to run out. The fats were extracted by chloroform and heat and fractional distillation. Their iodine index was found to be high. A study of the sections indicates an infiltration rather than cellular degeneration. The theory of a malassimilation of fats rather than a transformation by degeneration has been advanced also for phosphorus intoxication and supported experimentally. Gilbert and Carnot have apparently shown that the infiltration begins in the endothelial cells, which later transfer fatty droplets to the fixed-tissue cells. A similar rôle is probably played in tuberculosis. It is noteworthy that the most marked hepatic insufficiency is associated with the fattest livers, showing itself by an elevation of the quotient of incompleted nitrogenous metabolism (ureogenic), acidosis, hyperamino-aciduria, etc. Although our knowledge of fat metabolism in the body is inexact, there is general accord in assigning the liver an important rôle. The fats apparently have to be modified before being oxidized, and the liver is assumed to have the power of transforming saturated to unsaturated fatty acids, which are more readily oxidized. When the oxidation processes are slowed or interfered with, these unsaturated fatty acids accumulate. Another factor which must be considered is suprarenal insufficiency, which Neubauer believes important in phosphorus poisoning, but has not been the subject of precise study in tuberculosis. Three processes then appear to operate in fat metabolism in the tuberculous: (1) impaired organic oxidation, (2) suprarenal insufficiency, and (3) transportation of reserve fat to the liver.—*Étude chimique de la bile du foie des tuberculeux, R. Monceaux, Rev. d. l. Tuberc., June, 1925, vi, 305.*—(*A. P.*)

Pressure Relations in Pleural Space.—Aside from the action of the thorax itself, there are other factors, such as the function and size of the heart, or the gastrointestinal distention, which have a definite action upon pleural pressure. As a result of experiments it is concluded that, in spite of the presence of a fluid or gas in the pleural space, the diaphragm elevates, and the mediastinum can be deviated toward the healthy side even in the presence of a negative pleural pressure. As long as pressure is negative, with fluid or gas accumulation a compression of the diseased lung cannot be considered. The diaphragm only becomes depressed in the presence of fluid or gas in the chest, when the pleural exceeds the abdominal pressure.—*Zur Frage der Druckverhältnisse im Pleuraraum, A. Genersich, Beitr. z. Klin. d. Tuberk., 1924, lix, 634.*—(*H. J. C.*)

Blood Cholesterin in Tuberculosis.—The cholesterin of the blood serum in tuberculosis patients has no relation to the

clinical form or activity of the lesions. The figures obtained were within the limits of those found in normal subjects.—*La cholesterine du sérum sanguin chez les tuberculeux, Jullien and Martin-Rosset, Meeting, Réunion Biologique de Lyon, June 15, 1925, reported in Presse Méd., July 4, 1925, no. 53, 898 — (E. H. K.)*

Serum Calcium in Tuberculosis.—The amount of calcium in the serum of normal people is constant, and does not depend upon diet or the administration of calcium. In chronic tuberculosis the body strives to maintain calcium at a normal level, but just before death the values change and may be above or below the normal.—*Der Serumkalkspiegel bei Lungentuberkulose, W. Zimmermann, Deutsche med. Wchnschr., May 23, 1924, l, 686.—(H. S. W.)*

Blood Sugar in Pulmonary Tuberculosis.—The methods of Hagedorn and Jensen were used for the study of cases of chronic pulmonary tuberculosis, which had obtained for 15 hours from carbohydrates in the recumbent position. The figures for blood sugar in tuberculous individuals during fasting varied within normal limits. The administration of 20 gm. of glucose in severe cases of tuberculosis resulted occasionally only in a prolongation of alimentary hyperglycemia, which can be viewed as an indication of disturbance of the liver function. Muscular exercise for a half-hour after the administration of 20 gm. of glucose to mildly tuberculous patients caused no change in the curve. In severe cases of tuberculosis two reaction forms occurred: (1) a retarded rise in the curve and a prolonged duration of the hyperglycemia during rest, and (2) a diminution in the hyperglycemia and more rapid fall in the curve. The former is explained as an increase of the blood sugar as the result of asphyxia, while the latter is the result of glycogen poverty of the tissues. No definite relation between the severity of the disease and the finding could be noted. The findings only indicate that in chronic tuberculosis there is a disturbance of the blood sugar relation.—*Blutzuckeruntersuchungen bei chronischer Lungentuberkulose. W. Landau and O. Glogauer, Ztschr. f. Tuberk., 1925, xliii,* 121.—*(H. J. C.)*

New Constituent of Blood in Tuberculosis.—A new chemical substance has been found in the red blood cells. It contains *N* and *C* in the relation of N_2C_7. It is present in normal blood, and in the blood of the tuberculous it is greatly increased.—*Ueber einen auffälligen chemischen Blutbefund bei Tuberkuloseerkrankungen, A. Leimdörfer, Wien. klin. Wchnschr., December 4, 1924, xxxvii, 1256.—(H. S. W.)*

Magnesium and Calcium in Blood of Tuberculosis Patients.—This paper contains some observations regarding the magnesium content of the blood of normal people and people with pulmonary tuberculosis; it also gives the calcium content of the blood. Determinations were made on the bloods of 24 people, using the method recently described by Dienes. The calcium and magnesium determinations were made both on the blood and blood plasma, the plasma being obtained by centrifugating the cooled blood. For controls the red-blood-cell residue was also analyzed, which, together with the values obtained from the plasma, enables one to calculate the values for the whole blood. In normal and tuberculous persons the magnesium content of the blood plasma was found to vary from 0.018 to 0.026 mgm. per cc. and from 0.031 to 0.038 mgm. for the whole blood. No connection with the pathological condition or the age, stature and body-weight was found. The calcium values, determined by ashing the blood plasma of normal persons, proved similar to the values found by others, using a similar method, but were found to be usually considerably less in the blood plasma of tuberculous patients.—*The Magnesium Calcium Content of the Blood and Blood Plasma of Tuberculous Patients, E. M. Schoenheit, Am. J. M. Sc., November, 1925, clxx, 689.—(J. S. W.)*

Leucocytes in Pulmonary Tuberculosis at High Altitudes.—A review of the literature indicates that, in general, ideas do not agree concerning the leucocytes in pulmonary tuberculosis. Opinions regarding the eosinophiles are more in accord, and high counts are considered prognostically favorable. A neutrophilia usually parallels aleucocytosis. Most authors see a parallellism between neutrophilia and immunity to infection. In spite of absence of pyrexia and good general condition a marked disturbance of the neutrophiles indicates that pulmonary tuberculosis has not healed. An increase of lymphocytes indicates improvement, while lymphopenia, associated with high fever and caseous processes, is a bad omen. In the last 10 years there have been few observations on the monocytes. Very few authors have paid attention to the influence of other factors besides the pulmonary tuberculosis on the leucocytes. Numerous observations have been made on the effect of altitude, when in males the total count reaches the lower limits of normal, while in women it is

slightly higher. The neutrophiles are diminished, in men more than in women; lymphocytes and monocytes are increased relatively and absolutely. The author's own results led to the conclusion that the leucocyte count is higher the more favorable the case, eosinophiles are relatively diminished in the unfavorable group, and neutrophiles are normal in the mild cases while in severe cases they increased. The monocytes were found especially increased, which is attributed to the influence of altitude and its associated factors of sunlight. The favorable influence of altitude upon tuberculosis is considered intimately related with an influence on the monocytes.—*Untersuchungen über das weisse Blutbild Lungentuberkulöser im Hochgebirge, zugleich ein Beitrag zur kritischen Bewertung des weissen Blutbildes, N. Moszczytz, Beitr. z. Klin. d. Tuberk., 1924, lix, 128.*—(*H. J. C.*)

Leucocytes in Allergic States.—The delayed skin reaction in rabbits (Arthus phenomenon) possesses some features in the common with the tuberculin skin reaction in guinea pigs in that both are delayed in onset and are characterized by similar macroscopic lesions, edema, erythema, induration and often necrosis. It seemed, therefore, desirable to study by the supravital staining method the behavior of reacting leucocytes during intrapleural anaphylactic reactions in both animals. For the purpose a small series of rabbits were sensitized by multiple intraperitoneal injections of horse serum. Twenty-one days after the initial injection pleural exudates were induced in six animals, three sensitized and three controls, by intrapleural injections of 5 cc. of sterile hormone broth to which 0.3 cc. of horse serum has been added. The cells of the resultant exudates were examined twenty-four hours later by supravital neutral-red and Janus-green staining in a constant-temperature box. In the sensitized rabbits the leucocytes were found to be largely killed, a small number of the polynuclear neutrophiles only being found alive. No dead leucocytes were found in the exudate from the controls. As results with guinea pigs sensitized with horse horse serum were unsatisfactory, a series of 5 guinea pigs were sensitized by two intraperitoneal injections of chemically pure crystalline egg albumin. Eighteen days after the last injection, pleural exudates were produced in the usual manner in four of the animals and twenty-four hours later 0.8 cc. of egg albumen solution was added to the performed exudate. Two control animals were similarly treated. No dead cells were found in the exudate either before or subsequent to the administration of the antigen. In order to verify the sensitization, one guinea pig was given 1 cc. of the antigen intravenously after the pleural tap had been made; the animal died a typical anaphylactic death in about five minutes. On guinea pig received a small amount of antigen intrapleurally in order that any delayed reaction might be studied. At the end of twenty-four hours, the fluid contained only living cells. In several rabbits in which a pleural exudate was produced with hormone broth and 1 cc. of horse serum added to the exudate twenty-four hours later, only iving cells were found in the fluid from twenty to thirty minutes thereafter. Summarizing the above results, it will be seen that in rabbits the leucocytes are killed after control with the antigen for twenty-four hours, but not after a shorter period, that is, thirty minutes. In guinea pigs, on the other hand, the leucocytes are not injured at either period. The sensitized guinea pig, under ordinary conditions, reacts immediately and transiently on reinjection of the antigen intracutaneously, and usually does not give a delayed skin reaction. The sensitized rabbit, on the other hand, never gives an immediate skin reaction, but does give a delayed skin reaction which is usually much more than transient. Whatever the explanation of this difference in type of reaction may be, in the above experiments an analogous condition as regards their leucocytes apparently holds true, that is, the leucocytes of guinea pigs are uninjured by antigen whereas those of the rabbit are killed. In a previous article the authors have shown that in a tuberculin-reactive guinea pig, the leucocytes are killed on contact with tuberculin for twenty-four hours. Here we are dealing with a delayed reaction, and the analogy with a rabbit sensitive to horse serum, giving a delayed reaction, whose leucocytes are killed by the antigen, is evident.—*A Supravital Study of Leucocytes in Allergic States: A Comparison of Delayed and Immediate Intrapleural Anaphylactic Reactions, P. H. Long and F. W. Stewart, Am. J. Path., January, 1926, ii, 91.*—(*J. S. W.*)

Fate of Leucocytes in Tuberculin Reaction.—In the tuberculin and in the reinfection reaction, the leucocytes forming the bulk of the exudate are polymorphonuclear, and, so far as is known, the polymorphonuclear leucocyte phagocytizes tubercle bacilli but does not destroy them. Consequently, the rôle played by these cells in the reaction is problematical. It has seemed desirable to know whether the leucocytes themselves share in the general sensitization of the tuberculous animal, and the present study is concerned with this point. One

method of demonstrating sensitization is to show whether or not the supposedly sensitized cell undergoes necrosis when exposed to specific agents, in this case tuberculin, which to the cells of normal animals are innocuous. The condition of the cells can be determined by supravital staining with neutral red and Janus green following the technique of Sabin. A series of guinea pigs was sensitized by the injection of killed tubercle bacilli into the peritoneal cavity. Three injections, each 2.5 mgm. dry weight of bacilli, sufficed, as shown by the intracutaneous tuberculin skin test and the examination of the exudates. The latter was obtained as follows: Two guinea pigs, one sensitized and one control, each received 4 cc. of hormone broth containing 0.1 cc. of old tuberculin into the right pleural cavity; no immediate reaction resulted save for a temporary series of hiccoughs. Twenty-four hours later portions of the exudates were withdrawn, using carefully cleaned and warmed glass tuberculin syringes. A drop of the exudate was placed on a coverslip, and inverted on the dye-treated slide, and transferred to a microscope in a warm-box maintained at a temperature of 37 to 38°C. Fluids from control and sensitized animals were placed on the same slide, to avoid errors due to the concentration of dye or other possible difficulties. This procedure was repeated at forty-eight hours and, in some instances, again at seventy-two hours. In the supravital preparation cell injury is denoted by rounding of the cells, together with a cessation of the streaming motions of the granules. Then as the cell dies there is gradual diffusion of the neutral red throughout the protoplasm of the cell, together with a concentration of the granules, vacuoles, mitochondria and nuclear material in the centre of the cell. The nucleus is deeply stained, whereas in the living cell it is unstained. *Results:* In the exudates obtained from the sensitized guinea pigs, twenty-four hours after the administration of the tuberculin, *living* cells were never found, whereas the control normal guinea pig receiving tuberculin at the same time showed no *dead* cells. The sensitized guinea pigs averaged from 80 to 90 per cent polymorphonuclears in the exudate, whereas the controls tended to show lesser amounts. In the exudates removed from the sensitized guinea pigs at forty-eight hours only about one-half the polymorphonuclears were found dead. The other forms of cells were all alive. At seventy-two hours no dead cells were found. One pair of guinea pigs received a suspension of killed tubercle bacilli instead of tuberculin. Results were similar but were more delayed. At twenty-four hours only about one-third of the polymorphonuclear cells were dead, whereas at forty-eight hours all forms of cells were found dead. At seventy-two hours only a very small fraction of the polymorphonuclears were dead. No dead cells were found in the exudate from the control. *Conclusions:* In the tuberculin and reinfection reactions in tuberculin-hypersensitized animals, the reacting inflammatory cells appear to be themselves sensitized. Treated with appropriate doses of antigen they undergo early death. These first cells are gradually replaced by others probably reacting largely to the presence of necrotic tissue. The newly emigrating cells are viable elements. Further study is required to determine the immunological significance of these facts.—*The Fate of Reacting Leucocytes in the Tuberculin and Reinfection Reactions, F. W. Stewart, P. H. Long and J. I. Bradley, Am. J. Pathol., January, 1926, ii, 47.*—(*J. S. W.*)

Blood and Vegetative Allergy.—There was a direct relationship between the blood changes and the irritability of the vegetative nervous system. There existed the well-known lymphocytosis of tuberculous processes of slight extent, as well as a leucocytosis in progressive cases.—*Blutbild bei Tuberkulose in Beziehung zur vegetativen Allergie, O. Halir and A. Kettner, Beitr. z. Klin. d. Tuberk., 1924, lx, 52.*—(*H. J. C.*)

Tissue Extracts in Tuberculosis.—The places of residence and of production of the substances that contribute to the defense of the host in tuberculosis have been the subject of many investigations, including the relation of the fixed tissues to defensive processes. In the latter connection, perhaps more attention has been paid to the occurrence of protective or bactericidal substances in tuberculous tissues than in normal tissues. However, there is some evidence for the belief that the tissues of the non-tuberculous animal possess a well marked "native" defense power against the tubercle bacillus, and that certain types of normal tissue possess this power in a greater degree than do others. The studies reported here are concerned with the effects of fresh extracts of various organs of normal rabbits on rabbits infected with tuberculosis. These animals were inoculated, some with human and some with bovine tubercle bacilli, the majority receiving 10 mgm. subcutaneously between the scapulae, although a few received 0.1 mgm. of the bacilli intravenously per kgm. of body weight. The organs chosen for the experiments were lung, kidney, spleen, liver, suprarenal and heart. In rabbits the lungs are most commonly the site

of demonstrable disease (tuberculosis), while the heart is involved with extreme rarity. Concentrated extracts were made from these various organs under aseptic precautions, and these extracts were filtered through fairly coarse filter-paper, tightly stoppered and stored in the icebox. All filtrates were used for inoculation from one to nine days after preparation; the injections being done subcutaneously in the anterior abdominal wall in 0.2 or 0.25-cc. amounts. A number of animals received organ extract on the eighth day before injection of tubercle bacilli subcutaneously, followed by an immediate second inoculation of organ extract. Another smaller group was treated with organ extract the day following intravenous injection of tubercle bacilli, a second inoculation of organ extract being given eight days later. The largest number of animals was inoculated with organ extracts one day and eight days after subcutaneous injection of tubercle bacilli. The extracts of different kinds of organs were found to vary considerably as to the amount of influence displayed. Extracts of suprarenal and lung frequently would seem to retard the development of the disease, those of heart and liver produce less effect as a rule while extracts of spleen and kidney exert little or no influence. The freshness of the organs used, the short time utilized in preparing the extracts, the avoidance of incubation and the preservation of the extracts at icebox temperature, make it seem possible that the more or less protective substance present in some of the organ extracts exist in the organs before removal from the animal. Better results were obtained when the organ extract was given following the injection of bacilli than when given preceding the infection of the animals. The order of the organ extracts in effectiveness does not correspond with the order of the organs in the control animals as to the relative lack of suspectibility to tuberculosis.—*Extracts of Normal Tissues in Experimental Tuberculosis, R. S. Austin, J. Infect. Dis., September, 1925, xxxvii, 256.*—(*J. S. W.*)

Intrauterine Inoculations of Acid-Fast Bacilli.—In the usual methods of subcutaneous, intraperitoneal or intravenous injections of microörganisms for experimental purposes, the latter are distributed over a diffuse area, in which their fate in many cases escapes control after a relatively short time. By confining them to a restricted and isolated space they should be more readily accessible to examination under variable experimental conditions. For this puspose it would be necessary to select a cavity which could be isolated without serious consequences to the individual. The uterine cavity seemed to be the most suitable for this method, and therefore suspensions of tubercle bacilli were injected into the ligated segments of the uterus of the guinea-pig. For the experiments both virulent and avirulent bacilli were used. The uterus in the anesthetized guinea pig was exposed and, through the application of three ligatures, two segments were demarcated in one of the uterine horns. The upper ligature was tied firmly, and the uterus thus separated from the fallopian tube. A complete transverse incision was then made just below the lower of the three ligatures, and the uterine horn separated from the cervix. The opening into the horn was surrounded with pledgets soaked in mercuric-chloride solution, and through the opening about 0.1 or 0.2 cc. of the suspension of bacilli was injected into the upper segment, the lower ligature being tied firmly around the needle and tightened after removal to prevent the escape of any of the inoculum. The cut end of the uterus was finally cauterized to destroy any bacilli that might be adherent to the opening of the divided uterine horn when the needle was withdrawn. Following this the abdominal wound was closed. Altogether, 113 guinea pigs were used in the experiment, of which 66 received intrauterine injections and 47 subcutaneous injections for comparison. In a certain number of animals, which had previously received subcutaneous or intrauterine injections of the nonvirulent strains, a second injection was subsequently made with the virulent or nonvirulent bacilli, in order to determine whether, as the result of the first injection, immunity had been produced. The results obtained with the intrauterine method, as compared with the generally used subcutaneous, intraperitoneal or intravenous inoculation, show that the former is followed by extensive, localized, well-encapsulated lesions at the point of inoculation in which the bacilli persist for at least three months noncontaminated in the exudate; while in the latter such persistent localized and encapsulated lesions are not found. Thus it is possible to produce considerable localized chronic lesions with acid-fast bacilli, which otherwise would call forth only transitory elusive changes. Both intrauterine and subcutaneous injections of virulent tubercle bacilli are followed by generalized tuberculosis. Notwithstanding the great difference in the general effects which follow intrauterine injection of the virulent and nonvirulent bacilli, both microörganisms persist in the uterine cavity approximately equally well, and both are taken up by leucocytes; but with the nonvirulent bacilli the lesions remain localized,

while with the virulent bacilli they extend to other organs. The presence of chronic lesions produced by nonvirulent bacilli did not lead to an immunity against a subsequent injection of either virulent tubercle bacilli or nonvirulent bacilli when injected subcutaneously one or two months following the first inoculation in relatively large doses. It is suggested that the method of intrauterine inoculation might prove of interest in the study of other virulent microorganisms, the fate of which after ordinary methods of inoculation it is difficult to follow.—*Intrauterine Injection of Acid-Fast Bacilli in the Guinea Pig, Y. C. Sun, O. Ishii and L. Loeb, J. Infect. Dis., December, 1925, xxxvii, 528.*—*(J, S. W.)*

Tuberculous Infection of Testicle in Guinea Pigs.—Stewart and Petroff showed that Koch's intraperitoneal phenomenon, Pfeiffer's phenomenon and Paterson's pleural reaction could be produced in animals sensitized by dead tubercle bacilli. To extend this study, it seemed desirable that the work on allergic manifestations in the testes of infected animals, reported by Long and Seyfarth, be reinvestigated in animals sensitized by dead tubercle bacilli. Twenty male guinea pigs were employed, and one-half of these were sensitized by repeated intraperitoneal injections of killed (boiled) tubercle bacilli, the untreated guinea pigs serving as controls. When the injected animals showed a definite intracutaneous reaction to 5 per cent old tuberculin, all animals received 0.1 mgm. dry weight in saline suspension, of bovine tubercle bacilli in the right testis. Animals were killed 48, 72 and 96 hours, and 5, 6, 7, 9, 14, 21 and 28 days after infection. Testes from both control and sensitized guinea pigs were fixed and sectioned microscopically, and an attempt was made to analyze the tissue in respect to the various histological features of the reactions, for the purpose of contrasting the two series. The results seem to indicate that the difference between control and sensitized are mainly those of degree. The sensitized react more acutely; polymorphonuclears appear in greater numbers; endothelial leucocytes appear early in the disease in greater numbers; necrosis occurs earlier; and fibroblastic reaction of marked degree precedes that of the control. However, the prominent feature observed in the sensitized early in the process, a feature not appearing in early controls, is necrosis of epithelial structures. This necrosis is the complicating factor in the evolution of such reactions as marked polymorphonuclear invasion and endothelial and fibroblastic proliferation. It cannot be determined whether this is a "protective earlier generation of tubercle" or an ordinary reaction to necrosis. Every histological characteristic of the sensitized testis, though to a less degree, may be encountered in the control testis before the intracutaneous test has become positive, and, in consequence, no one histological feature may be said to characterize the reaction to reinfection in the testes of an animal generally sensitized to tuberculin. The differenences are only those of degree. After the sixth day little or no difference is seen between control and sensitized. Eventually, caseation occurs in both. In this series it was not shown that sensitization with killed bacilli has any protective value; in fact, the controls showed rather less disease. The above conclusions apply to a given organ, a given method of sensitization, and to a certain infecting quantity of the bovine strain of tubercle bacillus.—*Testicle Infection in Guinea Pigs Sensitized with Killed Tubercle Bacilli, F. W. Stewart, J. Immunol., February, 1926, xi, 123.*—*(J. S. W.)*

Intravenous Injections of Oil in Rabbit.—At four-day intervals over a period of two months, 0.5 to 2 cc. of purified, bleached olive oil, of purified olive oil, unbleached, and finally of paraffin oil, were injected intravenously into rabbits. Since pulmonary sclerosis was never observed, even microscopically, it is concluded that purified olive oil cannot of itself produce sclerosis, but that when this occurs it must be attributed to the product which is added to it, as a vaccine or an antiseptic.—*Étude expérimentale des injections intraveineuses d'huile chez le lapin, G. Caussade, A. Tardieu and A. Grigaut, Meeting, Soc. de Thérapeutique de Paris, April 8, 1925, reported in Presse Méd., April 18, 1925, no. 31, 503.*—*(E. H. K.)*

Carbon Dioxide and Growth of Acid-Fast Bacteria.—There is some doubt as to the necessity of the presence of carbon dioxide in cultivating tubercle bacilli and other microörganisms. While it has been generally conceded that the growth of bacteria cultivated over alkaline solutions in closed spaces is greatly inhibited, this effect has been explained as being due to a dehydration of the nutrient medium by the alkali, rather than to the removal of carbon dioxide. Experiments were done to throw further light on this point. Saprophytic and virulent tubercle bacilli were grown over acid (sulphuric) and alkali solutions in tightly sealed receptacles. In some instances 30 per cent glycerol or calcium chloride was used as the dehydrating agent.

To limit the production of carbon dioxide by the bacteria themselves the following conditions were observed in the production of the medium: 1. The medium used must contain no carbohydrates or other fermentable substances, such as glycerol. If growth is not possible without their presence, their amount must be reduced to the minimum which will sustain growth. 2. The protein content must be reduced to the minimum since bacteria produce a certain amount of carbon dioxide from proteins. 3. The inoculum must be as uniformly and as thinly seeded over the medium as possible, since clumps or clusters of microörganisms seem to be able to retain the carbon dioxide, which they produce even in the presence of a carbon-dioxide absorbent. 4. The medium must be adjusted to a reaction sufficiently acid to make the carbon dioxide available for the microörganism, and more easily removed by the absorbent. Actual formulae are not given. Under various conditions uniformly consistent results were observed. Growth was always inhibited over alkaline solutions, although the media were less dehydrated than those incubated over acid, on which good growths were obtained. Hence the inhibition of growth of various strains of tubercle bacilli, when incubated over alkali in closed spaces, cannot be explained as being due to dehydration of the nutrient medium, since growth occurs over other equally or more efficient dehydrating agents which are not carbon-dioxide absorbents, such as sulphuric acid, carbon dioxide and glycerol. The only explanation which can account for this phenomenon is that carbon dioxide, in some way, is a vital factor in growth.—*Carbon Dioxide as a Factor in the Growth of the Tubercle Bacillus and Other Acidfast Organisms, G. E. Rockwell and J. H. Highberger, J. Infect. Dis., January, 1926, xxxviii, 92.*—(*J. S. W.*)

Complement Fixation in Tuberculosis with Antigens from Acid-Fast Saprophytes.—Acid-fast saprophytes defatted with trichlorethylene or tetraline, reacted as antigen with the serum of tuberculous rabbits. The antigenic activity varied greatly with preparations from different saprophytes. Water and milk bacilli, which furnish potent antigens in reactions with human serum, were feeble in reactions with serum from infected rabbits. The results following the addition of lecithin to the antigen were highly irregular. The activity of antigens prepared from smegma, blind-worm and trumpet bacilli was increased. The activity of turtle-bacillus antigen was greatest when the bacilli were defatted with tetraline without the addition of lecithin. The timothy bacillus furnished a much better antigen when extracted with trichlorethylene with the addition of lecithin than when extracted with tetraline with or without lecithin. The reactions were at their maximum 3 to 4 weeks after infection of the rabbit. These results confirm the hypothesis previously presented that quantitative rather than qualitative differences exist between the structural elements of the acid-fast saprophytes and true tubercle bacilli.—*Untersuchungen über Komplementbindung bei Tuberkulose. II. Ueber die Beziehung zwischen Antigen und säurefesten Saprophyten und dem Serum tuberkulöser Kaninchen, T. Ogawa, Ztschr. f. Immunitätsforsch. u. exper. Therap., September 15, 1925, xliv, 218.*—(*E. R. L.*)

Effect of Lead on Experimental Tuberculosis.—Rabbits were injected with lead solutions or (a few) fed with lead until a basophilia resulted, and were then inoculated with tubercle bacilli. The administration of lead was continued, some of the rabbits dying spontaneously. No difference in the amount or distribution of the tuberculosis could be determined at autopsy between the lead-treated and normal control rabbits. A quantitative analysis of the lead in the lungs of some of the animals showed no relationship of lead content to the amount of tuberculosis.—*Tuberkulose und Bleivergiftung, K. Kisskalt and F. Schütz, Deutsche med. Wchnschr., May 23, 1924, l, 678.*—(*H. S. W.*)

Diet in Experimental Tuberculosis.—Guinea pigs infected with tuberculosis were fed with various diets. Those high in fat rendered animals less susceptible to various infections including tuberculosis. In guinea pigs fed with lemon juice as an antiscorbutic nutrition was improved and the animals became quite fat. They survived normal controls when infected with tubercle bacilli. Codliver oil administered to guinea pigs with extensive tuberculosis not only failed to help, but caused acceleration of the process. Normal animals excreted codliver oil through the skin, and developed a spastic gait and nervous symptoms.—*Tuberkulose und Ernährung, B. Leichtentritt, Deutsche med. Wchnschr., May 23, 1924, l, 672.*—(*H. S. W.*)

Complement Fixation with Antigens from Acid-Fast Saprophytes.—Partigen *A* prepared by the method of Deycke and Much from butter, water, milk, smegma, trumpet, blind-worm and timothy bacilli, on injection into rabbits stimulated the production of substances fixing complement with the homologous antigen, and occasion-

ally with similar partigen from other acid-fast bacilli. Injection of rabbits with partigens *F* and *N* did not lead to the production of complement-fixing bodies corresponding to these antigens.—*Untersuchungen über Komplementbindung bei Tuberkulose. III. Ueber die antigenen Eigenschaften der aus saurefesten Saprophyten hergestellten Partialantigene und das Verhalten der entstehenden Stoffe im Komplementbindungsversuch, T. Ogawa, Ztschr. f. Immunitätsforsch. u. exper. Therap., September 30, 1925, xliv, 403.*—(*E. R. L.*)

Serological Identity of Human and Bovine Tubercle Bacilli.—This investigation was undertaken to supplement the previous work of Tulloch and his collaborators, and to verify their contention that human and bovine tubercle bacilli are identical serologically. The series investigated include 31 bovine strains isolated from animal lesions, all except four by direct cultural methods, and 22 bovine strains isolated from human lesions, all except three by direct culture methods. For control purposes a series of eugonic strains from human surgical lesions, which had been previously investigated serologically, was examined with the bovine strains. Immune sera were obtained by inoculating rabbits with ether-acetone extracted human and bovine tubercle bacilli. The route of inoculation is not mentioned. Antihuman tubercle serum was obtained in this way with a titre of 1 in 1600. Some difficulty was experienced in producing antibovine serum on account of the greater toxicity to the rabbit of the bovine bacillus, but eventually a serum of a titre of 1 in 800 was obtained. Suspensions of bacilli for the agglutination experiments were made as follows: Emulsions were prepared from cultures grown on Dorset's or Lubenau's egg medium, extracted with acetone and ether, dried, ground up into a paste with 1.4 per cent sodium bicarbonate, and then suspended in physiological saline solution with phenol added up to 0.5 per cent. If carefully prepared, these suspensions remain stable for over a week. Of each strain to be tested, 1 cc. of a suspension standardized to contain 32,000 million microörganisms per cubic centimetre, and 1 cc. of antiserum in a strength equal to 16 times the titre, were mixed, and set at room temperature. The supernatant fluid was used for the absorption of agglutinin tests which were run in varying dilutions carefully controlled with normal rabbit serum. Results were fully tabulated and show that: *1.* Practically every strain is agglutinable to the full titre by both human and bovine sera, and all are agglutinable by the serum one and one-half times the titre of these type sera. *2.* Practically every strain absorbs all the agglutinin from a dilution of either serum equal to four times the titre, and all strains absorb all the agglutinin from either serum diluted to twice its titre. This investigation confirms the findings of other investigators that tubercle bacilli of the human and bovine types are not distinguishable by agglutination or absorption of agglutinins.—*The Serology of the Bovine Type of the Tubercle Bacillus, W. M. Cumming, Tubercle, December, 1925, vii, 105.*—(*J. S. W.*)

Anaerobic Growth of Tubercle Bacilli.—Tubercle bacilli, when exposed to *Bacillus putrificus* for as long as nine days, lost their capacity to grow in culture media. Animals inoculated with cultures of tubercle bacilli thus exposed for a long time, and later with cultures exposed for a shorter time, were living and well seven months after the inoculation.—*Ueber die Lebensdauer der Tuberkulosebazillen in Kulturen anaerober Fäulnisbakterien, F. Passini, Wien. klin. Wchnschr., October 29, 1925, xxxviii, 1182.*—(*H. S. W.*)

Viability of Tubercle Bacillus.—Many experiments have been done to determine the bactericidal effect of sunlight on the tubercle bacillus. But no reference to the exact penetration of the ultraviolet rays into mucoid matter, such as sputum, has been found. Sputum is often extremely tenacious, and its ability to protect the tubercle bacillus is well recognized. To determine the bactericidal effect of sunlight at Tucson, Arizona, on sputum from advanced cases of tuberculosis, such sputum, in amounts approximating those most likely to be expectorated, was placed in Petri dishes containing sterile dust and exposed to direct sunlight for various periods up to seventy-two hours. For an exposure of seventy-two hours sputum was first exposed April 2nd and was not ready for inoculation until April 23. While not undergoing exposure the dishes were covered, and kept at room temperature in the dark. At the end of each period of exposure, healthy guinea pigs were inoculated in duplicate with a suspension of the sputum and dust through a pocket made subcutaneously on the left side near the inguinal nodes. Six guinea pigs received sterile dust alone and six more served as uninoculated controls. The general opinion to-day is that the tubercle bacillus is killed in from twenty to twenty-five minutes to two hours to two and one-half days depending upon the amount of sunlight and other conditions. The results of the experiment outlined above indicate that tubercle bacilli in sputum exposed to direct

sunlight, in a manner to simulate as closely as possible actual community conditions, are viable for longer periods than is generally conceded. Guinea pigs inoculated with sputum exposed to sunlight for two, three, four, five, six, twelve, twenty, twenty-five, thirty, forty-eight and seventy-two hours showed extensive tuberculous infections.—*Viability of Mycobacterium Tuberculosis in a Semi-Arid Environment, M. E. Caldwell, J. Infect. Dis., November, 1925, xxxvii, 465.—(J. S. W.)*

Synthesis of Tyrosine and Tryptophane by Tubercle Bacilli.—Mammals, in distinction to the higher plants, cannot build up tryptophane synthetically. Tubercle bacilli which had been grown on tyrosine and tryptophane-containing glycerine-bouillon, as well as those grown on tyrosine and tryptophane-free asparagine, contained 1.1 per cent troptophane and 1.4 per cent tyrosine. This indicates that tubercle bacilli possess the property of building aromatic amino acids out of aliphatic compounds, thus resembling the higher plants in the property of cyclopoiesis.—*Über den Tyrosin- und Tryptophangehalt von Bouillon- und Asparagintuberkelbacillen. Ein Beitrag zur Frage der Cyclopoiese durch Bakterien, H. Popper and J. Warkany, Ztschr. f. Tuberk., 1925, xliii, 368.—(H. J. C.)*

Polymorphism of Tubercle Bacillus.—Human tubercle bacilli from homogeneous liquid cultures of Arloing grown on potato jelly assumed in twenty days remarkable filamentous shapes. At times these filaments were 15 or 20 times as long as normal bacilli, while again they formed a much subdivided mycelium. These filaments are only slightly acid-fast and do not take the gram stain well. Occasionally they appear very granular. When transplanted to the usual media they again assume normal shape and staining properties.—*Polymorphisme du bacille tuberculeux: formes myceliennes ramifiées, F. Arloing and A. Dufourt, Meeting, Section d'Études Scientifiques de l'Oeuvre de la Tuberculose, June 13, 1925, reported in Presse Méd., July 4, 1925, no. 53, 896.—(E. H. K.)*

Influence of Light on Growth of Tubercle Bacilli.—Human tubercle bacilli, grown on a modified Wassermann's medium (consisting of 15 cc. horse serum, 3 cc. glycerine and 30 cc. distilled water, heated for 15 minutes on the water-bath, filtered, sterilized in the autoclave for 20 minutes, and mixed with 2 per cent agar and 1 per cent peptone) were tested to determine the influence and various effects of light. In order to observe the changes produced by the light itself upon the medium, rayed media were coincidently seeded. Sunlight passing through the glass of the tube required 1 to 1½ hours, when of an intensity of 120 HSE, to sterilize the culture completely. Mild temperature changes had no influence. Arc light, especially the pure white, containing ultraviolet and green light, acted almost identically. On the contrary, roentgen rays, as well as β and γ rays of radium were without action. In large doses all of the bactericidal light-rays caused alteration in the medium, which played a part in the destruction of the bacilli by sunlight.—*Zur Frage des Einflusses der Strahlenenergie auf das Wachstum der Tuberkelbacillen in vitro, M. Friedland, Centralbl. f. Bakt., 1925, xcv, 404.—(H. J. C.)*

Bacteriolysis of Tubercle Bacilli.—Bacteriolysis was found to occur under the influence of hot alkalies as well as acids. In the cold even concentrated nitric acid did not completely dissolve the bacilli. Experiments with pepsin and trypsin, and organs and organ extracts, resulted negatively. Likewise intraperitoneal injection into guinea pigs proved negative. A complete solution was only observed after 30 days' treatment with lactic acid at 37° after pepsin digestion of benzoyl-chloride treated bacilli, and 2 hours' hydrolysis with hydrogen peroxide in the autoclave at about 150°. Markedly variable results were obtained with 5 different strains handled in identical manner.—*Zur Bakteriolyse der Tuberkelbacillen, W. Blumenberg and W. Möhrke, Ztschr. f. Hyg., 1925, cv, 186.—(H. J. C.)*

Tubercle Bacilli in Bile.—In veterinary medicine the presence of tubercle bacilli in the bile, even in the absence of macroscopic tuberculous changes in the liver, has been known for years. The author found bacilli in guinea pigs and human beings in about 50 per cent of the cases, and believes that the incidence is actually higher than this, and that the low findings are attributable to the present inefficient methods of investigation. Löwenstein's view, that the bacillemia becomes more frequent with progression of the disease and that every death from tuberculosis is associated with a genuine bacillemia, is concured with.—*Über die Ausscheidung von Tuberkelbacillen mit der Galle, T. Koizumi, Ztschr. f. Tuberk., 1924, xli, 173.—(H. J. C.)*

Sections through Cultures on Potato Media.—It was demonstrated by sections across colonies of human, bovine, avian and fish bacilli on potato media that the

colonies do not penetrate the interior of the media. Between the surface of the potato and the inner surface of the colonies there is a nebulous zone, where there are no bacilli and which is entirely blue-staining. The bacilli assume a frankly acid-fast aspect only in the most superficial layer of the colonies.—*Aspects des coupes des cultures de bacilles tuberculeux sur pomme de terre, F. Arloing and Malaitre, Meeting, Soc. de Biologie de Paris, June 27, 1925, reported in Presse Méd., July 4, 1925, no. 53, 893.—(E. H. K.)*

Antigenic Substances of Bacterial Cells.—The progress of immunological knowledge has been impeded by the tendency to apply all the facts ascertained by the study of coaguable proteins, such as horse serum, egg white, etc., by direct analogy to the reactions induced in animals infected or treated with bacteria. The further understanding of the biology of bacterial infection and immunity requires more precise knowledge concerning the bacterial antigenic substances which, in quite obvious chemical properties, differ from the antigenic true proteins. None of the bacteria studied in the past contains any considerable amount of heat-coaguable albumin or globulin. These materials are probably always present to a slight extent in bacterial extracts, and may determine the limited formation of antiprotein antibodies and, consequently, of true anaphylaxis. But they do not represent the predominant antigenic constituents of the bacterial cell. These are apparently represented by the "nucleoprotein" and "residue substance" fractions. The former comprises the bulk of the extractable bacterial substance and is of protein nature, but is not an ordinary coagulable protein. Nucleoprotein is antigenic, being capable under certain conditions not only of reacting *in vitro* with antibodies, but also of inducing antibody formation when injected into animals. It is probably a mixture of a number of substances not functionally separable up to the present time. The residue substance, on the other hand, is relatively heat-stable, gives no protein reactions; is alcohol-precipitable, and its structure is apparently that of a complex carbohydrate. Biologically, this substance is precipitable, and gives complement-fixation reactions with homologous antibodies, but is apparently incapable of inducing antibody formation. In attempts to obtain a better understanding of the relationship between these antigenic fractions of the bacterial cell, a series of animals (rabbits) were immunized with whole bacteria and nucleoproteins, filtered and unfiltered, obtained from tubercle bacilli, streptococci, and pneumococci, and a comparative study of the antibodies obtained was made. The materials used as antigens for precipitation tests were the respective whole material, nucleoprotein and the residue materials. It was found that the antiserum produced with whole material (tubercle bacilli) had little precipitating powers for the nucleoprotein material, but precipitated whole material and residue, whereas that produced by the injection of nucleoprotein material precipitated all three substances. When the nucleoprotein is filtered free of any traces of bacterial fragments no antibody to the residue is formed. This was also found true of an antiserum produced by immunization with filtered streptococcus nucleoprotein. Immunization with the nucleoprotein, if such nucleoprotein is rendered free from bacterial bodies or fragments of bacterial bodies by Berkfeld filtration, incites the production only of antinucleoprotein antibodies which, as previous studies have shown, are species-specific but are not type-specific to the same degree as residue antibodies. Immunization with dissolved residue alone leads to no antibody formation whatever. This residue is believed to represent the haptophore group upon which specificity depends and which, in the simple process of solution, is disrupted from another substance in combination with which it represented a complete antigen in the antibody-forming sense. The formation of specific antiresidue antibodies is apparently dependent on the injection of morphologically formed elements, at least, as far as experiment can determine at the present time. While antiresidue antibodies are formed only when such undisrupted bacterial cell substances are present in the immunizing substance, immunization with whole bacteria, even when attempts are made to preserve them from solution by treating with formalin, leads to the formation of both antiresidue and antinucleoprotein antibodies, probably because a certain amount of solution inevitably takes place after injection within the animal body. It is probable that the residue haptophore group is split off from the nucleoprotein, which may be regarded as its mother substance, and the antigenic complex of the whole bacterial cell consists of a combination of nucleoprotein and residue material in which the residue determines the specificity of the total.—*Studies on the Antigenic Substance of the Bacterial Cell, H. Zinsser and T. Tamiya, J. Exper. M., September 1, 1925, xlii, 311.—(J. S. W.)*

Standardization of Tuberculin.—The need for a standard by which tuberculin can

be measured quantitatively is obvious. Tuberculin in some form is used in large quantities in the diagnosis of tuberculosis, yet a diagnostic test or therapeutic injection is yet to be made with a measured quantity of the active principle. The reason is that no preparation containing the active principle and nothing else has ever been made, and, furthermore, we do not know what the active principle of tuberculin is. Chemical assay being out of the question we have been forced to fall back on some biological method. The methods used at present in the standardization of tuberculin may be grouped as (1) those based on the action of tuberculin on the hypersensitive tuberculous animal, such as the lethal-dose methods and skin-test methods, and (2) those based on the interaction of tuberculin and serum antibodies in the serum of a tuberculous animal, as the precipitin and complement-fixation tests. While each of the methods within these groups has its individual advantages, the disadvantages are great in all of them. The method by which the minimum lethal dose of a tuberculous guinea pig is determined is altogether too coarse, too many unknown factors being concerned. The method by which the ultimate dilution giving a cutaneous test in a tuberculous guinea pig is determined is unreliable because of the wide individual variation in skin-reaction capacity in tuberculous guinea pigs of the same series. The precipitin and fixation reactions between tuberculin and the serum of a tuberculous horse or horse inoculated with dead tubercle bacilli are unsuitable as standardizing methods because we have no assurance that the substance in raw tuberculin which reacts with the serum of the inoculated horse is the active principle of tuberculin. In fact, there is much evidence that it is not, and that the reaction which does take place is the result of interaction between serum antibodies and bacillary substance in the tuberculin, which cannot be properly called the active principle; that is to say, the substance which elicits the tuberculin reaction. A method is proposed which is based on the hypersensitiveness of the spermatocytes of the tuberculous guinea pig to the action of tuberculin. The spermatocyte reaction (previously reported as the "testicle reaction") is delicate, and will detect about one-tenth of the minimum quantity detectable by the skin test. To elicit this reaction tuberculin is injected directly into the testicle of a tuberculous guinea pig, and the effect upon the tubules and germ-cells is studied. If microscopic sections are made three weeks to a month after the injection of the tuberculin the following will be noted: Marked atrophy has occurred, the tubules being no more than half their original size. Spermatocytes and spermatids, together with spermatozoa, have disappeared. The tubules remain lined by their basement membranes and a single layer of epithelial cells. This characterizes the typical tuberculin spermatocyte reaction. On the basis of this test, a tuberculin unit suitable for measuring doses may now be defined as follows: The spermatocyte unit is that quantity of tuberculin just sufficient to abolish spermatogenesis in the majority of tubules on injection in a volume of 0.1 cc. into the testicle of a 400-gm. guinea pig with a mild, localized tuberculosis of one month's duration. Dilutions are made so that the 0.1 cc. injected represents from 0.1 to 0.00001 cc. of the unconcentrated tuberculin, diluted in tenths. Microscopic section of the testicle (middle cross section) one month after the injection of one unit or more, shows the majority of the tubules atrophic and lined only by spermatogenes. No normal spermatocytes, spermatids or spermatozoa are present. The test is controlled by the examination of the noninjected opposite testicle and of the injected testicle of a noninfected animal, both of which should show normal spermatogenesis. For rapid work, when sufficient time for embedding or cutting sections is not available, a rough approximation of the true result can be obtained by a simple procedure. The injected and the noninjected testicles are each cut in half and the fresh surface rubbed on microscopic slides. The slides smeared with the normal testicle will show numerous spermatozoa. Those smeared with the injected testicles show none or few or many spermatozoa in proportion to the degree of change in the testicle. The last slide in which spermatozoa are still hard to find may be considered to represent the injection of one unit. The unit so defined should be useful in standardizing tuberculin for diagnosis and treatment. Ordinarily, unconcentrated tuberculin, like *BE*, will be found to contain at least 1,000 spermatocyte units per cc., while OT will contain at least 10,000 units. The advantages of the above standardization method are: (1) the absolute specificity of the reaction, (2) the great delicacy of the reaction, (3) the sharp picture presented by the positive reaction, (4) the constancy of the reaction, and (5) the ease with which a permanent record of the reaction may be preserved. The chief disadvantages are the length of time desirable before reading the reaction (3 to 4 weeks) and the necessity of cutting, staining and examining sections. The latter disadvantages may be avoided by the use of the rapid method, but such a procedure is open to the

possibility of error.—*Standardization of Tuberculin: Assay on the Basis of the Spermatocyte Reaction, E. R. Long, J. Infect. Dis., October 1925, xxxvii, 368.—(J. S. W.)*

Standardization of Tuberculin.—A joint investigation by observers working independently was undertaken, to determine whether tuberculins found variable by the official Frankfurt test on guinea pigs, would also give comparable results by other methods of testing. These included guinea pig injection, cutaneous and subcutaneous, human cutaneous tests, the intracutaneous test on tuberculous cows, and particularly the precipitin or flocculation test of Dreyer and Vollum. These tuberculins were studied, one full strength, Frankfurt standard, and two having very low "tuberculin" values, namely 2 to 5 per cent and 5 to 10 per cent. The results showed a very definite agreement in all the tests except the precipitin method. This test does not necessarily measure the active principle of tuberculin, on which its use in the various methods of diagnosis of tuberculosis depends. Satisfactory agreement in the precipitin unit value was obtained by two different groups of workers by the precipitin test. This test apparently measures with a considerable degree of accuracy a substance probably other than the active principle of tuberculin, and presumably the interesting precipitable substance of Mueller and Laidlaw. The "tuberculin" value of tuberculins which have been standardized by the official Frankfurt method cannot in all cases be deduced from the precipitin test.—*The Standardization of Tuberculin and the Precipitin Test, C. C. Okell, H. J. Parish, R. A. O'Brien, G. Dryer, R. L. Vollum, S. L. Cummins and J. B. Buxton, Lancet, February 27, 1926, ccx, 433.—(J. S. W.)*

Active Principles of Tuberculin.—Work undertaken to determine authoritatively the protein or nonprotein nature of the substance in tuberculin, to which is due its specifically toxic reaction in the body of the tuberculous animal, has revealed the fact that the cause of the skin reaction is probably but not surely a protein. It is also now known that the specific precipitin reaction and the skin reaction given by old tuberculin are attributable to two separate substances present in this material. For example, if a solution of old tuberculin is treated under appropriate conditions with pepsin or trypsin for some time, it gradually loses its power to give a skin test, which power finally completely disappears, leaving the precipitating property with immune serum unimpaired. From large quantities of old tuberculin prepared from synthetic (protein-free) media, the author obtained considerable amounts of the protein or skin-toxic fraction and the carbohydrate residue antigen (precipitating fraction). The latter also acted as an antigen in the complement-fixation test, as one would expect from the now generally accepted relationship between fixation and precipitation. Hence, methods which have been suggested for the standardization of tuberculin by precipitin or complement-fixation reactions should be revised. Details are given of the preparation of the protein fraction, and its activity as compared with O. T. is discussed. The partly purified product, as obtained in 1-10,000 solution, gave skin reactions of approximately the same intensity as are given by the 1-100 solution of O. T.—*A Chemical Study of the Specific Elements of Tuberculin, I, J. H. Mueller, J. Exper. Med., January 1, 1926, xliii, 1.—(J. S. W.)*

Non-Protein Gum from Tuberculin.—A non-protein gum has been isolated from filtrates of human tubercle bacilli grown on a synthetic medium. This material is similar to the "residue antigen" of Zinsser and "specific-soluble substances" of Heidelberger and Avery. The gum also corresponds very closely to the material which Laidlaw and Dudley obtained from whole tubercle bacilli. No attempt has been made to immunize rabbits with this product, as it was assumed that, as in the case of other similar materials with which this has been tried, it would be without effect. However, it fixes complement and precipitates in high dilution in the presence of homologous immune serum, but fails to give a skin test in tuberculous animals. The preparation and some of the chemical properties of this substance are described in the article.—*A Chemical Study of The Specific Elements of Tuberculin, II, The Preparation of Residue Antigen from Old Tuberculin, J. H. Mueller, J. Exper. Med., January 1, 1926, xliii, 9.—(J. S. W.)*

Focal Tuberculin Hypersensitiveness.—In a previous study it was found that guinea pigs reacted with fibrosis to testicular infection with bovine tubercle bacilli before giving positive intracutaneous tuberculin reactions. This fact raised a question as to whether or not an animal with testicular infection would react to tuberculin introduced into the infected organ before giving a positive intracutaneous reaction to a like dilution. To test this question a series of guinea pigs were given 0.25 mgm. of living bovine tubercle bacilli in suspension. The B1 strain was used, and the right testis in-

fected. On the second, third, fourth, fifth, sixth, seventh and eleventh days after infection, 0.1 cc. of 5 per cent old tuberculin was injected into both the infected and normal testes, and a like quantity was given intracutaneously. Animals were killed about eighteen hours after the testing, and both testes were removed for histological examination. To eliminate the factor of trauma, in a second series both testes were infected with similar doses of the same bovine strain; two, four, six, seven and eight days later, one testis was tested with 5 per cent tuberculin, the intracutaneous test was performed, and the second testis received an equal amount of physiological salt solution. These animals were killed and the testes examined as in the first group. As a control, a single uninfected animal was given tuberculin in one and physiological salt solution in the other testis. Definite focal reactions, characterized by a sharply demarcated zone of increased necrosis of tubules, surrounded by a dense exudate of polymorphonuclear leucocytes, occurred in the infected organs before positive skin tests were obtained. In this study a positive intracutaneous reaction refers to one with at least central blanching, peripheral erythema and induration. Physiological saline-infected testes showed no reactions histologically save for the early evidence of infection. The significance of the earlier focal hypersensitiveness in an infected organ is wholly problematical. It probably means merely a more intense local flooding with antigen, but can have no bearing on the question of local origin of antibodies or of local immunity. Focal changes as a result of the tuberculin injected were first noted in the guinea pig receiving tuberculin on the third day after the infection.—*Observations on Focal Tuberculin Hypersensitiveness in an Infected Organ Previous to a General Sensitization, F. W. Stewart, Am. J. Path., September, 1925, i, 495.*—(*J. S. W.*)

Inflammation Due to Allergy.—Right-sided thorocoplasty was performed on a case three years previously, and the patient died of hyperplastic tuberculosis of the intestines. Autopsy findings were fibrotic phthisis of the right apex, with small cavities in the lower lobe and the lower part of the upper lobe, and pea-sized yellowish-white foci, which were surrounded by hyperemic areas. These foci consisted histologically of central caseation surrounded by alveoli in which a marked diapedesis was occurring. The circumfocal hemorrhages were considered to be toxogenic, resulting from a circumfocal inflammation occasioned by a tuberculin-like action. The condition is viewed as a fourth stage of tuberculosis, similar to the second stage, which results from hypersensitive reactions and leads to the development of focal inflammation or its equivalent, hemorrhage. Hemorrhage, in place of inflammation, represents a hyperergic reaction.—*Zur Morphologie der circumfokalen Veränderungen bei Lungentuberkulose, W. Pagel, Beitr. z. Klin. d. Tuberk., 1924, lix, 261.*—(*H. J. C.*)

"Vegetative" Allergy in Tuberculosis.—According to Guth, there exists a definite relation between pulmonary tuberculosis and the vegetative nervous system, which is determinable with the progression of the disease through changes of reactivity, especially in the behavior of the sympathetic toward the parasympathetic system. The author used subcutaneous adrenalin injections experimentally, and studied the effects upon the blood pressure and pulse, classifying these into five reactions or types. A comparison of these curves with the clinical findings, which are expressed graphically by the author, revealed that the changes of reactivity of the vegetative nervous system paralleled, in two-thirds of the cases, the extent and severity of the disease. There is a progressive diminution of irritability of the vegetative nervous system, first, of the sympathetic and then of the parasympathetic part, up to complete absence of reactivity. The prognostic value of the blood-pressure-pulse curve after adrenalin is of immediate value only, since in one-third of the cases other constitutional factors enter. Tests with pilocarpin disclosed equally interesting points. An elaboration of the experiments, by utilizing the sedimentation reaction, the blood picture, the complement-fixation reaction of Besredka, and, in individual cases the hemoclastic crisis, leads to the conclusion that tuberculosis has a definite action upon the entire vegetative nervous system and that the term "vegetative allergy" is justified.—*Vegetative Allergie, E. Guth, Beitr. z. Klin. d. Tuberk., 1924, lx, 39.*—(*H. J. C.*)

Cutaneous Tuberculin Reactions.—The time of their appearance, as well as their intensity, is of interest in tuberculin reactions, which may be classified as follows: (1) late and feeble reactions, appearing after twenty-four, thirty-six or forty-eight hours; (2) average reactions, appearing after six to twenty-four hours with persistent, well-marked induration; and (3) marked and early reactions appearing after five or six hours and becoming a veritable phlegmon. Of 200 acutely ill nontuberculous patients, 78 per cent gave a positive tuberculin reaction,

nearly all feeble and late. In undoubtedly tuberculous patients the reaction was positive in 97 per cent, strong and early in 12 per cent, and in the rest average and early. In tuberculous pleurisy 87 per cent gave a strong and early reaction. As to its prognostic value, all that one can say is that the reaction is very feeble or absent in tuberculous cachexia.—*Intérêt de la cuti-réaction précoce à la tuberculine, F. Bezançon and Vigneron, Meeting, Section d'Études des Scientifiques de l'Oeuvre de la Tuberculose, February 14, 1925, reported in Presse Méd., March 18, 1925, no. 22, 358.*—(*E. H. K.*)

Intravenous Injections of Tuberculin.—Koch's idea that tuberculin given intravenously produces more marked reaction than by subcutaneous administration was verified. A difference in reaction time between subcutaneous or intravenous injections was not found. Likewise, no difference was found in the different forms of pulmonary tuberculosis, whether tested by subcutaneous or intravenous injection. The course of the reaction also showed no significant differences.—*Studien zum Tuberkulinproblem. V. Mitt. Über die intravenöse Tuberkulininjektion, A. V. v. Frisch, Beir. z. Klin. d. Tuberk., 1924, lix, 306.*—(*H. J. C.*)

Effect of Tuberculin on Blood Protein.—The total protein content of the blood varies after tuberculin injections. In almost all cases changes in the blood protein occur after doses which occasion neither general, focal, nor local reactions. Likewise, the fibrinogen content changes under the same conditions. In the course of changes of the blood protein picture in the same individual, there are quantitative differences, but qualitatively the reaction is the same. A parallelism between the pyrexia and the fibrinogen curve does not occur in the same individual. To answer satisfactorily the question of the relation of the blood-protein reaction to special forms of pulmonary disease, many more examinations are required, although it appears that, in general, active processes cause an earlier increase of the fibrinogen content after tuberculin injections, while in latent or stationary processes the increase is less and more gradual.—*Studien zum Tuberkulinproblem. VII. Mitt. Tuberkulin-Reaktion und Bluteiweissbild, A. V. v. Frisch and S. Baumgartner, Beitr. z. Klin. d. Tuberk., 1924, lx, 163.*—(*H. J. C.*)

Protein Decomposition in Liver Due to Tuberculin.—The residual (noncoagulable) nitrogen content of the liver of tuberculous guinea pigs without widespread tuberculosis of the liver is greater than that of healthy animals. Subcutaneous tuberculin injections increased the residual nitrogen in the liver of tuberculous guinea pigs within six to eight hours, while the residual nitrogen content of the liver of normal guinea pigs is uninfluenced by tuberculin injections. Tuberculin injections in tuberculous animals occasion protein decomposition in the liver.—*Die Wirkung des Tuberkulins auf den Eiweissabbau in der Leber, R. Bieling and S. Isaac, Beitr. z. Klin. d. Tuberk., 1925, lx, 271.*—(*H. J. C.*)

Effect of Tuberculin Injections on Enuresis.—The conception of v.Kovats that enuresis in children was due to a disturbance of the endocrine system as the result of tuberculous intoxication, and that in these cases hilum adenopathy was present and the enuresis was an early symptom of tuberculosis, led to a retesting of this idea with almost negative results. Therapeutic tests, in treating cases of pulmonary tuberculosis with enuresis by means of tuberculin, had absolutely no affect upon the enuresis.—*Die Beeinflussung der Enuresis durch Tuberkulininjektionen, P. Müller, Ztschr. f. Tuberk., 1925, xlii, 294.*—(*H. J. C.*)

Trichophytin and Tuberculin.—Trichophytin is an extract made from some of the pathogenic hypomycetes. The human body that has had a mycotic infection reacts allergically to this product. With a superficial mycotic infection the administration of trichophytin usually will not bring about an allergic reaction, but the reaction does occur if the infection has been deep-seated instead of superficial. Twelve children with surgical tuberculosis, but having an additional mycotic infection, gave skin reactions to trichophytin. They were strongly allergic to Old Tuberculin. But old tuberculin does not produce reactions in nontuberculous children having mycotic infection. There is danger in treating tuberculosis with this product, as there is with other foreign substances, such as milk, caseosan, etc., for they may produce a recrudescence of an old dormant tuberculosis.—*Trichophytin und Tuberkulin, R. Peyrer, Wien. klin. Wchnschr., January 29, 1925, xxxviii, 147.*—(*H. S. W.*)

Tuberculin Reactivity Increased by Lipoids.—Reactions from O. T., as well as from individual partigens were increased by the addition of a nonspecific lipoid, and by the ether extract of human brain. The reactivity of neutral fats especially is increased by lipoids. Exposure of the mixture for 2½ hours to sunlight also increased

the reaction further. It becomes most marked when the mixture is exposed for ½ hour to X-rays. It is suggested that the X-rays cause activity of some of the previously inactive end-groups of the lipoid.—*Abgestimmte Reizsteigerung durch Lipoide, A. Ismet, Beitr. z. Klin. d. Tuberk., 1924, lix, 660.*—(*H. J. C.*)

Fat and Lipoid Antibodies in Tuberculosis.—According to Bergel the external layer of the tubercle bacillus is made up of acid-fast and alcohol-fast wax. This substance not only covers the tubercle bacillus, but also forms the outer layer of the inner granules. The intermediate substance between the individual granules consists of fatty-acid lipoid substances. The internal nucleus is composed of protein substances. It is reasonable, therefore, that this bacillus cannot be destroyed by protein antibodies. Much was the first, in 1909, to produce antibodies to the fats of the tubercle bacillus, and to *nastin*, the substance of the lepra bacillus. Fat antibodies could be found only in animals and men that had come in contact with acid-fast bacilli, or their constituents. Kleinschmidt was able to determine antibodies to chaulmoogra oil and in leprosy cases. Deycke, Much and Leschke showed that with fats or lipoids alone, as well as with proteins alone, a satisfactory immunization was not possible, but it was with all of them combined. Much's observations were corroborated by vonRuck, who unlocked tubercle bacilli with phenol, and then extracted them with alcohol and ether. With these antigens he found both fat and protein antibodies, in man as well as in animal. Meyer found lipoid antibodies after treatment with dead tubercle bacilli, but with tubercle-bacillus lipoids alone there was a weaker reaction to lipoid antibodies. Dienes and Schoenheit obtained no complement binding with lipoid antigen by treatment with protein extracts to tubercle bacilli. The findings of Meyer were verified by Boquet and Nègre, who believed that the fatty constituents insoluble in acetone and soluble in methyl alcohol were the best antigens for complement fixation in tuberculosis. Intracutaneous testing with partial antigens gave more reliable results, an insight into cellular resistance being, according to Much, the most significant. According to Miller, pulmonary tuberculosis cases are albumin-reactive, while surgical cases are fat-reacting. Adam found lupus to be fat-reacting. Deficient fat reactivity is found in progressive tuberculosis. Children with weakly developed fat reactivity are disposed to tuberculosis. Kögel considers an allergy to *F* and *N* favorable in severe cases, but a marked hypersensitiveness to *A* with weak fat reactivity is unfavorable. Drügg found a weak *F* and *N* reaction unfavorable in surgical tuberculosis. Ruppel, Bürger and Möllers opposed this entire view, and found no antigenic properties to these substances in guinea pigs, they believing the reactions due to contaminating bacterial protein. Müller and Much found that a tuberculous individual can react to tubercle-bacillus fat in a dilution 10,000-fold that occurring with proteins. Much and Adam found ether-alcohol lipoids from the guinea pig liver to produce no antibodies in rabbits because of the presence or inhibiting protein. After their removal antibody production occurred. Much believes the fat lipoid antibodies to be specific lipases. Frisch found a high lipase titre in favorable, and a low titre in unfavorable cases of tuberculosis. Grigaut found that the lungs of vaccinated animals possess six times the lecithin lipolyzing power of normal animals. According to Much the entire skin and connective tissue, as well as lymphocytes, produce the specific lipases. Müller found tuberculin efficient in increasing fat reactivity, at times more so than the partial antigens. Better results were obtained with radiant treatment, and especially X-rays increased the fatty-acid lipoid reactivity, artificial sunlight the nastin reactivity, and sunlight the total partial reactivity. According to Timm light therapy increases the *F* and *N* reactivity, and radium the nastin, while X-ray acts more in the sense of a nonspecific stimulant. Whether nonspecific lipoids and fats exert a therapeutic effect in producing fat-lipoid antibodies has not been determined. It is believed that antibodies toward lipoids and fats exist, and that they are of significance in the defenses against tuberculosis.—*Ergebnisse oder Übersichtsberichte. Fett- und Lipoid-Antikörper in inhrer Bedeutung für die Klinik der Tuberkulose. Eine Darstellung an der Hand der wichtigsten Literatur und nach eigenen Erfahrungen, H. Schulte-Tigges, Centralbl. f. d. ges. Tuberk.-Forsch., 1925, xxiv, 369.*—(*H. J. C.*)

Antibodies to Sheep Blood in Tuberculosis.—It has recently been shown that guinea pigs, infected with virulent bovine tubercle bacilli, develop much more antisheep amboceptor than controls given only the like amounts of sheep corpuscles. As there is no report of the effect of various types of tuberculosis in the rabbit on the formation of antibodies, experiments were done to determine the influence of such infection on the production of agglutination, lysins and precipitins for sheep blood. One

group of rabbits received virulent bovine tubercle bacilli intravenously, and another group avirulent human tubercle bacilli subcutaneously. In these groups the sheep blood was given intraperitoneally, either before, at the same time, or subsequent to the tuberculous infection, the necessary controls receiving sheep blood alone. A third group infected, some subcutaneously and some intraperitoneally, with avirulent human tubercle bacilli, received the sheep blood intravenously. The results are as follows: A rapidly fatal generalized tuberculosis in the rabbit from the intravenous injection of virulent bovine tubercle bacilli was without definite effect on the agglutinin and lysin content of the serum even to within a few days of death, while precipitin formation seemed to be slightly retarded. Local subcutaneous tuberculosis in rabbits produced by the injection of avirulent human tubercle bacilli ten to twenty-six days before the intraperitoneal injection of sheep blood had no appreciable effect on lysin or precipitin formation, but 2 of the rabbits given sheep blood forty-three days after injection maintained high specific lysin and precipitin titres for 200 and 445 days. Whether tuberculosis was the cause of this unusual reaction has not been determined, but similar results have been obtained in tuberculous guinea pigs. Rabbits infected subcutaneously with avirulent human tubercle bacilli, and given sheep blood intravenously at different intervals after infection, revealed slight variations from the usual course in antibody formation. Tuberculosis in the rabbit, either general or local, apparently has no marked influence on the antibodies that develop from the injection of sheep blood. In exceptional cases it may result in a prolongation of antibody accumulation in the blood.—*The Formation of Antibodies to Sheep Blood in Experimental Tuberculosis in Rabbits, L. Hektoen and H. J. Corper, J. Infect. Dis., July, 1925, xxxvii, 82.*—(*J. S. W.*)

Significance of Calcification of First Rib.—Wolff-Eisner adds 109 military cases and 47 cases from Davos to the previous 350 cases reported in the book of Kuthy-Wolff-Eisner. A special tendency of the first rib to calcify in tuberculous patients is not considered significant, for calcification is much more frequent among patients with emphysema and bronchiectasis. Of 109 cases reported calcification of the first rib occurred in 65 cases; in 5 it was early, in 6 it was slight, in 44 definite, in 7 slightly more so, and in 4 exceptionally so. Calcification of more ribs was found in 26 cases; beginning calcification in 2, slight in 5, marked in 15, slightly more so in 3, and exceptionally so in 1. Calcification of the cartilage of the first rib without coincident clinical or roentgenological apical tuberculosis was found 18 times. Calcification of the first rib on both sides, with apical tuberculosis on one side was found 8 times. In 19 cases of apical tuberculosis calcification of the first rib was absent. Of 47 cases at Davos calcification occurred in 24 (1 initial, 6 slight, 14 outspoken and 3 marked). Calcification of more ribs was found only once. Calcification without apical tuberculosis occurred five times. Apical tuberculosis occurred six times on side opposite to the cartilage calcification, and in 17 cases apical tuberculosis was present without cartilaginous calcification. There is no relation between apical tuberculosis and calcification of the cartilage of the first rib, nor is there any between the severity of the disease and the tendency toward healing. Calcification of the first rib, like arteriosclerosis, is considered a phenomenon of age, which afflicts the manual laborer earlier than the wealthy classes.—*Ist der Zusammenhang zwischen Verknöcherung der ersten Rippe und der Spitzentuberkulose (Freund-Hartsche Lehre) erwiesen? A. Wolff-Eisner, Beitr. z. Klin. d. Tuberk., 1924, lix, 300.*—(*H. J. C.*)

Deviations of Esophagus in Pulmonary Tuberculosis.—In studying deviations of the esophagus, the frontal rather than the oblique position, with the patient horizontal and with the hips slightly elevated, is the position of choice. The patient is given an opaque meal of pasty consistency, and this is observed fluoroscopically and roentgenographically. Deviation of the upper portion of the esophagus occurs commonly, and is generally associated with tracheal deviation. Deviation of the lower portion is less common, but may occur in cases of pneumothorax with effusion. Deviation of the entire esophagus is infrequent because of the relative fixation of the lower portion. Alterations of the normal shape or calibre of the organ occur frequently as localized narrowings or irregularities, or at times even enlargements. These may be present without dispacement of the organ. In the majority of instances these esophageal alterations are obviously to be attributed to the action on the mediastinal organs of contracting scar tissue of the lung and pleura. In certain instances there seems to be, in addition, a pushing over by the opposite lung. Positive diagnosis of esophageal alteration is possible only by fluoroscopic and radiographic examination, and can only be suspected in physical examination if there is a deviation of the trachea. Even the most

marked alterations give rise to no symptoms. The question is raised as to whether certain coughs associated with frequent vomiting may not have their origin in the irritation of the pneumogastric nerve caused by oesophageal displacement.—*Les déviations de l'oesophage au cours de la tuberculose pleuro-pulmonaire, E. Olbrechts and M. Paquet, Rev. Belge d. l Tuberc., April, 1925, no. 4, 109.*—(*E. H. K.*)

Displacement of Mediastinal Shadow.—A paradoxical type of cardiac deviation is described, dependent upon a fibrotic process in the right upper lobe of the lung, and occasioning a displacement of the mediastinum. The retraction of the scar tissue in the lung pulls the heart to the left side, with elevation at the cardiac apex at the same time. Similar conditions in the left lung cause a deviation of the mediastinal shadow to the midline of the cardiac shadow. If, at the same time, pleuritic adhesions pull on the other side, there is an oblique position of the heart. The author calls this a *phthisische Knickung.—Knickung des Mittelschattens bei cirrhotischer Oberlappenphthise im Röntgenbilde, A. Rad, Beitr. z. Klin. d. Tuberk., 1925, lxi, 636.*—(*H. J. C.*)

Early Signs of Tuberculosis.—Chilliness, obesity appearing between 20 and 25 years, special sensibility to toxins, serums, vaccines and autohemotherapy, frequent headache with asthenia and hypotension, instability of temperature between 37° and 37.5°, chronic enteritis of the mucomembranous type and dental caries are considered as a group of symptoms of tuberculous origin. There may be no clinically demonstrable tuberculosis present, but severe physical or mental strain may cause a sudden flareup of serious disease.—*Les petits signes de tuberculose, Nigoul-Foussal, Meeting, Académie de Méd. de Paris, May 12, 1925, reported in Presse Méd., May 16, 1925, no. 39, 647.*—(*E. H. K.*)

Parenchymal Râles in Pulmonary Tuberculosis.—There is a type of râles, small or medium, but uniform in size, bubbling, crackling, or crumpling in character, elicited toward the end of forced inspiration or bursting with the expiratory cough, and continuing during the greater part of the following inspiration. This is the common type of râle elicited over tuberculous lesions, and designated at times as indeterminate, creptitations, cracklings, or fine and medium râles. They are localized and constant, regardless of the quantity of the patient's expectoration. They remain unchanged, irrespective of how much the patient coughs or raises during the examination. A cough is often necessary to elicit them. They occur in showers always at the same phase of respiration. They are encountered in all the pathological types of tuberculosis. They have been named "typical indeterminate" râles by Bushnell. The lesions may caseate and progress; they may fibrose and heal; perifocal reactions may develop and subside; pleural adhesions may be present or absent; the patient may have severe constitutional symptoms or none at all; he may have considerable cough with profuse expectoration, or no cough and no expectoration; the roentgen ray may show any type of tuberculosis, and the involvement may be dense or it may be difficult to detect; still these râles remain unchanged and may persist indefinitely. Not infrequently, in time, as the lesions clear up and heal, the râles disappear, but there are many cases in which they persist after the patient has become clinically cured and the roentgen rays reveal fibrous tuberculosis. These râles have been compared with those known to be bronchial in origin and due to secretions in the bronchial tubes. There is no similarity. They have been compared with râles produced in normal lungs with no secretions in the bronchial tubes, the râles being undoubtedly caused by the inflation of collapsed lobules. A similarity was found to be present. They should, therefore, resemble atelectatic râles, examples of the latter being those elicited above pleural effusions or over areas of lung rendered atelectatic by obstruction of a bronchus or by compression. For the last two years, a study, for the purpose of determinating the mechanism of râles, has been made on cadavers. A bellows was inserted into the glottis and the cadaver made to breathe by inflating the lungs with the bellows. The chest was auscultated during this artificial respiration and râles if present were recorded. The lungs, larynx and treachea were then removed from the chest, and again by means of the bellows made to expand and collapse. Râles were again auscultated and recorded. Incisions were then made and the lungs and bronchi examined. So far, six different types of râles have been elicited. 1. A coarse, gurgling râle, heard over cavities, due to air passing through fluid in the cavities. 2. A rattling, which can be heard without the stethoscope, and due to fluid in the trachea and primary bronchi. 3. Medium râles heard throughout inspiration and expiration, and caused by fluid in the smaller bronchi. An incision over the area where the râles are elicited shows a bubbling of serum or fluid from the cut ends of the

bronchi during respiration and occurring synchronously with the elicitation of the râles through the stethoscope. 4. Sonorous and sibilant râles, like those heard in asthma, produced by tenacious fluid in the larger bronchi. 5. Fine and medium râles heard over normal lungs in which there are no secretions in the bronchi or bronchioles, and elicited only when the lungs are in a condition of collapse and from this point made to expand. They occur in showers toward the end of inspiration and are not heard during expiration. They are probably caused by a popping open of collapsed lobules as the air forces its way into the intralobular bronchioles, or possibly to a sudden separation of approximated walls of the bronchi during inflation. 6. Fine crackling and crepitant râles, heard over the surface of the lung when the bell of the stethoscope is pressed against the lung with some firmness and moved about. They are also heard during auscultation over the lungs and occur synchronously with the inflation of the subpleural lobules. Consequently it would appear that the "typical indeterminate" râles are connected in some way with the sudden expansion of partially or completely collapsed pulmonary lobules. This collapse might be due to an exudate or infiltration in a neighboring lobule, to the constriction or contraction of areas of fibrous induration, or to the occlusion of bronchioles by the pressure of inflammatory tissue, by the constriction of fibrous bands, or by the obstruction of plugs of mucus, etc. In other words, we have a condition of partial or relative atelectasis, made more complete by an expiratory cough, and thus the "typical indeterminate," or, better termed, *lobular* or *parenchymal*, râles are produced. *Summary and conclusions:* 1. Showers of fine and medium râles of equal size, occurring at the end of a full inspiration, or the so called coughing râles which occur when the patient forcibly breathes out, gives an expiratory cough, and immediately breathes in, are not due to the bubbling of secretions in the alveoli and bronchial tubes, nor are they necessarily associated with abnormal secretions in these structures Such râles are not always associated with active inflammatory processes in the pulmonary parenchyma or bronchi, and must be distinguished from treacheal, bronchial, cavity and pleural râles. 2. Parenchymal râles may be due to pneumonia, fibrosis, atelectasis, pleurisy, etc., and cannot be said to be associated with any particular disease or pathological condition. 3. Showers of râles usually elicited only by cough and heard over the upper parts of the lungs are unquestionably the most reliable physical signs for the detection of tuberculous lesions. 4. The significance of these râles as a criterion of manifest tuberculosis and the character of the lesion will depend on other clinical findings, on history, symptoms, sputum and roentgen-ray examination. A period of observation may be necessary in order to arrive at a definite diagnosis. 5. In studying the process of a case and in deciding whether a tuberculous lesion is progressing or undergoing retrogressive changes, the persistent occurrence of this type of râles is not a conclusive sign unless correlated with the physical signs and clinical findings.—*Parenchymal Râles in Pulmonary Tuberculosis. Their Clinical Significance, E. H. Bruns, J. Am. M. Ass., September 5, 1925, lxxxv, 739.*—(*J. C. D.*)

Changes in Leucocytes during Tuberculin Treatment.—Earlier studies on changes in the leucocyte picture following tuberculin injection as an index, frequently the only one, of tuberculin action, are verified (*Beitr. z. Klin. d. Tuberk., liii, 394*). Repeated examinations of the blood can indicate hypersensitiveness and overdosing, and therefore give this examination a definite value.—*Über die Veränderung des weissen Blutbildes im Verlauf der therapeutischen Tuberkulinanwendung bei Lungentuberkulose. Weiterer Beitrag zur Tuberkulinbehandlung, C. J. Raffauf, Beitr. z. Klin. d. Tuberk., 1924, lx, 31.*—(*H. J. C.*)

Leucocytes in Tuberculosis.—Tuberculosis produces various changes in the leucocytes. But it is a mistake to depend too much upon the blood picture in arriving at a diagnosis, particularly after only a single examination. If carefully used and interpreted, study of the blood will yield considerable aid in arriving at a diagnosis and prognosis.—*Das Hämogramm in der Tuberkulosebegutachtung, H. Dornnedden, Deutsche med. Wchnschr., May 23, 1924, l, 678.*—(*H. S. W.*)

Hemoptysis.—Hemoptysis occurred in 121 of 992 tuberculosis cases (12 per cent). Inquiry into the pathogenesis of this accident does not give a satisfactory explanation of its occurrence. The great frequency of a positive Wassermann reaction in tuberculosis patients who have hemoptysis is considered significant as indicating a causative relationship. The toxins of intestinal parasites are considered as another common factor. In general, hemoptysis is associated with disease elsewhere in the body. The presence of granular bacilli in those subject to hemoptysis gives to this variety of microörganism a clinical and prognostic significance.—*Hémoptysies, Melamet, Meet-*

ing, Soc. d. Méd. de Paris, June 12, 1925, reported in Presse Méd., July 4, 1925, no. 53, 895.—(E. H. K.)

Sputum in Various Forms of Pulmonary Tuberculosis.—That elastic fibres are alveolar or ring-formed in the exudative types of tuberculosis and cluster-like in the proliferative type was verified. Round cells were found in almost all sputum regardless of the pathological form of the tuberculosis. Fat-staining proved of no value as a diagnostic method, and doubly refractive substances determined by means of the polarization microscope gave no data of significance.—*Über den Auswurf bei den verschiedenen Formen der chronischen Lungentuberkulose, M. Madlener, Ztschr. f. Tuberk., 1924, xli, 257.—(H. J. C.)*

Increased Permeability of Blood Vessels as Cause of Hemoptysis.—It was formerly accepted that blood in the sputum in pulmonary disease, especially tuberculosis, meant destruction of a portion of the wall of a pulmonary vessel. More careful observation, however, often fails to confirm this. It is likely that the majority of pulmonary hemorrhages are due neither to ulceration of vessel walls nor rupture of aneurysmal dilatations. They occur and recur, especially with weather changes, the menstrual cycle and the presence of acute respiratory infections. They are usually small, but are sometimes copious. This tendency to blood-spitting during the menstrual period is a part of the general increase in severity of symptoms at this time, undoubtedly due to increased pathological activity in the tuberculous foci. According to the theory of Jobling and Petersen, when the enzymes accompanying the menstrual cycle enter the blood-stream, a portion of the anti-enzymes formerly bound to the tuberculolytic enzymes leave the latter to become attached to the former. The released tuberculolytic enzymes then cause increased tuberculous activity, which may manifest itself as increased capillary permeability with escape of blood. The relation between hemorrhages and pneumococcal and other respiratory infections was studied at the Phipps Institute, and is not infrequent. Browning studied the relation between weather changes and hemoptyses. Sudden alteration of barometric pressure, humidity and temperature, are all accompanied by increased incidence of blood-spitting. The toxins from the tubercle bacilli or other microörganisms may readily act as capillary poisons, causing increased permeability such as has been shown to occur from various chemical poisons. Weather conditions certainly affect physiologic conditions and demand considerable adaptation. Hemoptyses are especially frequent at the time of day when barometric pressure is lowest, namely at 4 A.M. and 4 P.M. *Summary: 1:* Acute infections of the lung are apt to produce their greatest effect where the tissues are already injured by tuberculous disease, causing increased permeability of tissues, including blood vessels. *2:* The menstrual enzyme in some way causes increased activity in local tuberculous processes, with probably also increased permeability. *3:* Certain weather changes affect all tissues, but especially those of a lung the seat of active disease, and increase the tendency to transudation of blood.—*Increased Permeability of Vessel Walls as a Frequent Cause of Pulmonary Hemorrhage, F. M. Pottenger, Am. J. M. Sc., September, 1925, clxx, 420.—(A. P.)*

Menstruation and Tuberculosis.—The menstrual period has a profound effect upon all the functions of the body, in that temperature, pulse, blood-pressure, muscular strength, reflex sensibility of the nervous system and other functions are increased, and that shortly before the onset of bleeding, or with its inception, they all rapidly diminish. Local and general symptoms are phenomena caused by the function of the ovary, and are regulated, not through the nervous system, but by products of internal secretion originating from the ripened follicle or the ruptured corpus luteum. Menstruation, according to the most recent views, is considered an abortion of the nonimpregnated egg. During the menstrual cycle symptoms are observed which, during the premenstruum, represent an increased sympatheticotony, and at the time of bleeding a vagotony. The sympatheticotony of a severely toxic tuberculosis case exhibits itself like the sympatheticotony occasioned by the corpus luteum; therefore in these cases amenorrhoea or oligorrhoea of various grades is observed. In vagotonic conditions the opposite is seen, that is, prolonged and more frequent bleeding, with increased uterine contraction, the socalled *essential dysmenorrhoea.* The latter, after elimination of the causative factors, is benefited by specific treatment. In the premenstruum definite temperature elevations are seen only in the sympatheticotonic cases of exudative type, while in vagotonic cases they are slight or lacking. The premenstruual elevation of temperature can persist with the persistence of the corpus luteum, or a pregnancy, even in the second week, can thus be definitely determined. Increase of body temperature with conception and increase of concomitant symp-

toms cannot be considered as an index of unfavorable progression of the tuberculosis, but rather as a shift in the endocrine balance. In examining the blood of tuberculous women the phase of the menstrual period must always be considered, whether the examination is for corpuscular elements or for molecular factors. The course of an hemoptysis is markedly dependent upon the menstrual period.—*Menstruation und Tuberkulose, S. Somogyisen, Beitr. z. Klin. d. Tuberk., 1924, lix, 609.*—(*H. J. C.*)

Menstrual Fever in Tuberculosis.—In the normal woman there is progressive premenstrual hyperthermia and menstrual hypothermia. In women with pulmonary tuberculosis there is observed a normal reaction in exaggerated form or an abnormal reaction with fever during menstruation. Amenorrhea may be "active" or "silent," the latter indicating that at the expected menstrual period there are no temperature variations, the former that this period is accompanied by definite symptoms and fever. In general, those with good prognosis exhibit the normal menstrual variations while those with doubtful prognosis present the abnormal febrile reaction. During febrile menstruation there may exist a bacillemia, as demonstrated clinically, pathologically, and by guinea-pig inoculation, with the patient's blood.—*Les fièvres menstruelles dans la tuberculose pulmonaire, J. Caussimon, Thèses de Bordeaux, 1925, reviewed in Presse Méd., June 13, 1925, no. 47, 794.*—(*E. H. K.*)

Menstrual Reaction in Tuberculosis.—Frequently during menstruation there is either a development of signs, such as râles in the lungs, that are not to be found at other times, or an extension of the signs already present. Symptoms likewise develop or become aggravated at this time. Sensitiveness to tuberculin is apparently unchanged. This reaction in a large number of cases was present in 77 per cent, and thus is quite an aid in diagnosis.—*Ueber die Verwertung der Mensesreaktion zur Beurteilung der Aktivität tuberkulöser Krankheitserscheinungen insbesondere der Lungen, H. Maendl, Wien. klin. Wchnschr., May 1, 1924, xxxvii, 440.*—(*H. S. W.*)

Vital Capacity in Citizens' Military Training Camp.—This study was made at an army summer training camp at Camp Meade, Maryland, July 1924. The purposes of the study were (1) to obtain accurate vital capacity estimations on a relatively large and homogeneous group; (2) to determine whether or not the improvement in general physical condition resulting from training is accompanied by a corresponding change in vital capacity, and (3) to determine, if possible, the value of the vital capacity estimation as a criterion of "general physical fitness." *Conditions and technique of study:* The subjects were all young white men, aged 16 to 20, coming from the states of Pennsylvania, Maryland, Virginia and District of Columbia. They were from both urban and rural communities and of various occupations (mostly students), and are believed fairly to represent healthy normal youths. They were almost invariably quite nude when examined. Observations were made on accurately calibrated spirometers of the water-seal type, delicately counterpoised, and graduated to 20 cc. Each man was given three trials to make a maximal expiratory effort. All the men were not tested, but they were "tagged" at random as they passed from the examining hall to the dressing-room. There were two series, one of 825 young men before, the other of 443 after, training. Among these were 103 who chanced to have observations made on both occasions. The main groups, however, are regarded as accurate cross sections of the entire 3,500 men. The vital capacity per square metre of body surface, according to Dubois and Dubois's formula was estimated. Measurements of chest circumference and expansion were also made, but not found of value. The tables show, for every age group, an increase both in actual expiratory output and in calculated cc. per sq. m. body surface. For the 103 men tested on both occasions the increases approximate 5 to 6.4 per cent. The opinion was formed from the observations that youths of the "long-waisted" type gave uniformly and often markedly higher readings than those of the same height but shorter chest conformation. For youths of a given height the expiratory output was roughly proportional to the length of the thorax. There was also a special company of 115 men "below par" on physical examination and efficiency tests, 84 per cent of whom were underweight according to army requirements. These men were under the detailed supervision of a medical officer and special line officers. They were not put through such arduous work, and were given more rest and extra nourishment. Every recorded observation on this group was definitely lower than for the normals, and at the beginning of training their expiratory output averaged nearly 15 per cent below the normal both at the beginning and conclusion of training, while their vital capacity in terms of cc. per sq. m. surface was 4.4 per cent below before and 5.1 per cent after training. It thus appears that the men of the special company were bene-

fited in roughly the same proportions as the men at large, the actual increase being from 6.3 to 5.4 per cent. *Conclusions: 1:* The actual maximum expiratory output of this class of normal white youths ranged from 4,100 cc. to 4,400 cc. with an average of about 4,200 cc. *2:* Their vital capacity in cc. per sq. m. body surface ranged from 2,400 to 2,500 cc. *3:* The course of training prescribed in an army summer training camp resulted for all age groups in an average increase of 5 to 6 per cent. This appeared to be related to their improved physical condition. *4:* The vital capacity of young men adjudged "below par" physically was found nearly 15 per cent below "normal" for actual output and 4.4 per cent for output per square metre body surface These differences remained after training, thus appearing to measure, in some degree at least, their general physical fitness.—*Vital Capacity in a Citizens' Military Training Camp, S. A. White and P. F. McGuire, Arch. Int. Med., September 15, 1925, xxxvi, 355.*—(*A. P.*)

Thoracic Pain in Early Tuberculosis.—While vague thoracic pain is more common in later stages of pulmonary tuberculosis, it does frequently occur as the first symptom. It probably represents pleural irritation. But the idea of a protective reflex fails to explain the origin or nature of the pain. Pain occurs at times in the precordial region, and is referred from the pleura, and is in no sense a cardiac pain. It occurs also in the shoulder at times with muscular atrophy of the part.—*Woher stammen die Schmerzen im Gebiete des Thorax bei beginnender Lungentuberkulose? I. Knotz, Wien. klin. Wchnschr., July 16, 1925, xxxviii, 813.*—(*H. S. W.*)

Pain in Pulmonary Tuberculosis.—Pain is a protective mechanism. In tuberculosis of the lung it is well known that the process may proceed to great tissue destruction without producing pain until the pleura becomes involved. On the other hand, a very early process that is in or under the pleura will produce pain or tenderness at certain points, particularly in the area of the proper intercostal nerve or in some area that is definitely in the "referred" path. Shoulder pain is frequently associated with early apical tuberculosis. Pain above the clavicle, in the shoulder joint or in the muscles of the upper arm, may come from a neuritis of the brachial plexus incident to an apical pleuritis. There may be pain in the neck and swelling of cervical lymph nodes on the side of the apical pleurisy. Also vague pain or sense of pressure beneath the sternum may be a feature of tuberculosis of the tracheobronchial lymph nodes. Precordial pain may also have its origin in this condition. Sharp pain in the shoulder or lumbar region, and a burning sensation in the lower dorsal region often accompany diaphragmatic pleurisy. This latter disease often is associated with apical tuberculosis, and the symptoms may simulate those of cholecystitis, appendicitis or gastric ulcer. These pains frequently become aggravated during menstruation and after tuberculin administration. Antipyretics, hydrotherapy, dry cuppings, local application of heat, etc., all help to alleviate the pain. Intravenous administration of *Attritin* also helps, as does also a small pneumothorax. Prognosis is generally better in patients with than in those without pain.—*Beitrag zur klinischen Bedeutung der Schmerzen bei Lungentuberkulose, A Schick, Wien. klin. Wchnschr., May 1, 1924, xxxvii, 444.*—(*H. S. W.*)

Muscular Pain in Pulmonary Tuberculosis.—Muscular pain was observed in two cases, but as a rule it is rare. In the first case, one of severe pulmonary tuberculosis with fresh basal pleuritis, there developed painful muscle cramps of one to two minutes' duration in the upper abdomen and lower thoracic regions of the afflicted side. The second case was one of previous phrenic exairesis and thoracoplasty, with at present progressive bilateral pulmonary tuberculosis, in whom all the muscles of the lower part of the chest, the back, and the upper part of the abdomen of both sides were affected.—*Über schmerzhafte Muskelkrämpfe im Bereiche der Thorakalnerven bei Lungen- und Pleuratuberkulose, P. Weissner, Ztschr. f. Tuberk., 1925, xliii, 455.*—(*H. J. C.*)

Psychic Fever Reactions in Tuberculosis.—Frequently patients experience somewhat prolonged elevations of temperature that may be attributed to psychic influences, such as the reception of visitors, failure of arrival of an expected visitor, receiving and writing letters or failure to receive letters.—*Zur Erklärung psychogener Fieberreaktionen bei Lungentuberkulosen, E. Ladeck, Wien. klin. Wchnschr., May 1, 1924, xxxvii, 439.*—(*H. S. W.*)

Psychology of Tuberculosis Patients.—Patients react variously when a diagnosis is made. One, when told that he has pulmonary tuberculosis, may react with an exaggerated juvenile response, failing to grasp the significance of the diagnosis, but seeing in it an opportunity to travel or go to new places for treatment, or he may believe that the diagnosis is incorrect. This type is more common in younger females.

Another patient may have a *shock reaction*, seeing his whole future blasted. He is quite pessimistic and depressed and fails to adapt himself to reason. It is more often the people of strong vitality who react in this way. Sometimes a patient becomes a *hypochondriac*, informs himself from an encyclopaedia as to symptoms, prognosis, etc., and in retrospect finds that he has had all the symptoms, which gives him further basis for pessimism. Some are *hopeful*, accepting the diagnosis willingly because it lays the foundation for proper treatment. They are optimistic. They know that many people have been cured and count themselves among them. A patient may be *hysterical*, expecting special treatment and consideration. He demands every advantage for himself and becomes the chronic sanatorium patient. Another may feel *aggrieved*. There are many other types of reaction, such as the religious fanatic, the reflective and rational, the economical (coldly counting the cost of the cure), the resigned, the fighting, the indifferent, those ashamed of the diagnosis and desiring to hide it, the self-reproachful, etc. The physician must know the type with which he is dealing and should take this knowledge into consideration, both in imparting to the patient his diagnosis and in treatment.—*Beitrag zur Psychologie des Lungenkranken, E. Stern, Deutsche med. Wchnschr., July 10, 1925, li, 1146.*—(*H. S. W.*)

Tuberculous Cachexia.—Although often a concomitant of tuberculosis, cachexia is frequently absent in this disease and present in other conditions. It frequently develops in enteric tuberculosis but is here an alimentary cachexia. It may also occur in patients with an atonic stomach associated with anorexia and vomiting, and may clear up as soon as the patient can again retain food.—*Einiges über die Kachexie Tuberkulöser, A. Kirch, Wien. klin. Wchnschr., May 1, 1924, xxxvii, 439.*—(*H. S. W.*)

Tintometer for Skin.—A pressing need in clinical medicine is an accurate method for measuring and recording the color of the skin. There is perhaps no other type of clinical examination subject to greater error, due largely to the inability of the physician to describe and match colors. From a large number of plaques representing artists' reproductions of skin color from approximately 100 normal and pathlogical subjects, a tintometer has been constructed which apparently covers adequately the entire range of color variations encountered in human skin in health and disease. The tintometer consists of multiple color scales each composed of ten plaques, representing progressive increase in color, each plaque of which has been analyzed qualitatively and quantitatively and expressed in three dimensions of hue, value and chroma. The normal range of variation has been first determined. A separate color scale has been constructed for jaundice, cyanosis, erythrosis and brown pigmentations, each resembling somewhat the Tallquist scale employed in the clinical determination of hemoglobin. By means of these tintometers direct comparisons with the color of the skin are made. While the method is subject to considerable error it offers marked advantages over the usual clinical descriptive method.—*A Tintometer for the Analysis of the Color of the Skin, L. G. Rowntree and G. E. Brown, Am. J. M. Sc., September, 1925, clxx, 341.*—(*J. S. W.*)

Diagnosis of Pulmonary Tuberculosis.—The differences between exudative and productive forms of pulmonary tuberculosis are discussed. Pure forms occur only rarely. Exudative phthisis requires absolute mental and bodily rest, while in productive forms stimulation by means of numerous therapeutic measures comes into consideration.—*Die qualitative Diagnose der Lungentuberkulose und ihre therapeutischen Konsequenzen, G. Rodenacker, Ztschr. f. Tuberk., 1925, xlii, 479.*—(*H. J. C.*)

Diagnosis of Pulmonary Tuberculosis.—According to von Hayek diagnostic efforts must take into consideration two requirements: first, the determination of the extent of the local process and its character, and, second, a "diagnosis" of the entire body in its capability to counteract the disease. From the standpoint of prognosis and therapeutic indications it is important to determine the resistance of the entire body.—*Zur "Entwicklungsdiagnose" tuberkulöser Lungenkrankungen, H. v. Hayek, Zeitschr. f. Tuberk., 1924, xli, 185.*—(*H. J. C.*)

Early Diagnosis of Tuberculosis.—It is doubtful whether there is any one serious disease which we come across more unexpectedly than pulmonary tuberculosis, and it is still one of the very common diseases. We shall never detect it in its incipiency by casual careless methods of examination, nor are its evidences confined to the chest. It is a systemic disease, and often presents many features to arouse suspicion. We are inclined from our early contact as students to view it too much in the light of physical signs. Tuberculosis is not a continuous illness, as a rule, but a relapsing infection, with slight manifestation fol-

lowed by periods of quiescence. A careful history is of the greatest importance, especially with regard to such incidents as pleural effusions, persistent cough for several weeks at a time, ischiorectal abscess or blood spitting. Connected with the history and of next importance are constitutional disturbances, such as slight malaise and fatiguability, slight irritability, loss of weight, or disturbance of temperature and pulse, or even slight digestive disturbances. The physical signs, generally speaking, have been exaggerated in importance and made too obscure. Lawrason Brown has done a great service to the profession in simplifying these. He gives as five cardinal evidences of tuberculosis: (1) positive sputum, (2) hemoptysis, (3) pleurisy with effusion, (4) localized râles on coughing above the level of the third rib, and (5) definite X-ray changes in this same area. If every doctor could hear a râle, and knew how to elicit it he would not be long in making a diagnosis. Positive sputum is important if present, but in these early cases is more often absent. Another important thing to remember is, that definite physical signs occur in healed or inactive tuberculosis. The presence of râles is not sufficient reason for sending a patient to a tuberculosis resort. Clinical common sense and judgment are, above all, needed. Also, certain nontuberculous conditions which simulate tuberculosis should be distinguished, especially postinfluenzal infections. In these cases the physical signs are usually extensive as compared with the X-ray findings, and the sputum never contains tubercle bacilli. Finally there are tuberculosis carriers, chronic fibroid cases usually in older people, who cough but are not sick and whose sputum may be loaded with tubercle bacilli, and cases of nontuberculous chronic bronchitis and peribronchitis, usually basal, associated with chronic sinus infection.—*The Respiratory System, J. A. Miller, in Symposium on Preclinical Signs of Disease, Med. J. & Rec., November 18, 1925, cxxii, 608.*—(*A. P.*)

Diagnosis of Activity in Pulmonary Tuberculosis.—There is no method of differentiating whether a case is undoubtedly inactive or active, and it is important to use numerous methods, especially the clinical picture in its entirety, and repeated laboratory tests. There are many cases of active tuberculosis in which prolonged treatment is not necessary, but in which prolonged observations are essential. The most important criterion for the appraisal of activity is a careful history. Less information is obtained from the clinical findings, and in well-established tuberculosis loss of body weight may serve as a sign of activity. The roentgen picture shows only the shadow of the present anatomic changes, but gives little or no information regarding the process. Definite fever can be viewed as a sign of activity, but hypochondriac, neurasthenic fever must not be confused with that of tuberculosis. A positive diazo and permanganate reaction is a sign of activity, especially when tuberculosis is otherwise proved. A negative reaction does not exclude activity. Of the specific allergic methods the Besredka reaction, which in early cases when positive indicates activity, and the tebeprotin test (with 0.1 mgm.) are considered valuable. The vegetative allergic methods of examination must be carefully utilized, but a single test is of very little value, while repeated or continuous tests may give conclusive evidence for or against activity. In progressive cases the determination of whether a case is still suitable for the treatment becomes important, and in this the physical findings assume an important position, especially when reinforced by vegetative allergic examinations.—*Die Aktivitätsdiagnose der Lungentuberkulose, E. Guth, Ztschr. f. Tuberk., 1925, xliii, 39.*—(*H. J. C.*)

Importance of History in Early Diagnosis of Pulmonary Tuberculosis.—If it is not possible, as yet, to diagnose the primary and secondary stages of tuberculosis, in which therapy should be initiated, then one must be satisfied with a "probability diagnosis," and of greatest aid in this is a careful history. As a result of unsatisfactory histories, tuberculosis is frequently not thought of. The favorite "grippe" is nothing more nor less than a flaring-up of an existing tuberculosis. A statistical study is presented, to show that 73 per cent of the patients entering the sanatorium were recommended for treatment too late. The practising physician must be educated to make an early diagnosis of tuberculosis and to recommend appropriate sanatorium treatment.—*Die Bedeutung der Anamnese für die rechtzeitige Erkennung der Lungentuberkulose, Gabriele Pohl-Drasch, Beitr. z. Klin. d. Tuberk., 1924, lix, 84.*—(*H. J. C.*)

Puncture of Lung in Diagnosis.—Puncture of the lung in pulmonary infections, especially with thickened pleura, has proved to be a very helpful method of diagnosis. The dangers of air emboli and pleural infection can be avoided by the use of a very small slender needle filled with salt solution.—*Ueber einen neuen Weg zur Differentialdiagnose der Lungeninfiltrationen, E. Czyhrlarz and E. Pick, Wien. klin. Wchnschr., May 14, 1925, xxxviii, 529.*—(*H. S. W.*)

Percussion of Apices of Lungs.—Individuals with moderate impairment at one apex (in tuberculosis) may be requested to breathe deeply four or five times. After this it frequently happens that for a few minutes the impairment disappears. This may lead to mistakes. If one gently presses on the apex in tuberculosis the impairment of the percussion note is accentuated, and the difference in the note over this region and over the normal side become more distinct.—*Ueber eine noch nicht beschriebene Beobachtung bei der Perkussion der Lungenspitzen, E. Czyhlarz, Wien. klin. Wchnschr., February 12, 1925, xxxviii, 195.*—(*H. S. W.*)

D'Espine's Sign. In rare cases of enlargement of the hilum lymph nodes D'Espine's sign is positive and therefore it is not advisable to discontinue the use of this diagnostic method.—*Das d'Espinesche Zeichen (zur Diskussionsbemerkung Brüneckes auf dem Tuberkulosekrongress Coburg 1924), K. Klare, Beitr. z. Klin. d. Tuberk., 1925, lx, 308.*—(*H. J. C.*)

Value of X-Ray of Chest in Tuberculosis Suspects.—One frequently sees patients presenting vague symptoms possibly attributable to tuberculosis. It is not always easy to decide in which cases to have X-rays taken. Routine chest plates on all first examinations mean an added expense which must be considered. The present study deals with 118 consecutive cases in the O. D. D. of the Peter Bent Brigham Hospital, Boston, of which 107 had X-rays taken. None had been seen before by either of the two examiners, whose examinations were made independently and a common diagnosis agreed upon after consideration of the history. Approximately thirty minutes were devoted to history and examination. The cases were divided into four groups as follows: *1:* Positive clinical diagnosis and positive roentgenogram. *2:* Positive clinical diagnosis and negative roentgenogram. *3:* Negative clinical diagnosis and positive roentgenogram. *4:* Negative clinical diagnosis and negative roentgenogram. Group 1 comprised 4 cases (3.7 per cent); group 2, 15 cases (14 per cent); group 3, 7 cases (6.5 per cent), and group 4, 81 cases (75.7 per cent). In addition, there were studied 500 cases observed in the hospital wards upon whom a diagnosis of pulmonary tuberculosis had been made, and the physical signs noted by various men under ideal conditions compared with the X-ray findings. Symptoms were classified as *primary* (pleurisy, cough, expectoration, night sweats, loss of weight), *secondary* (chest oppression, fatigue, malaise and nervousness), and *tertiary*, such as body pains, headache, indigestion, chilliness, dyspnea. In approximately 20 per cent of the cases there was disagreement between the clinical and X-ray findings from a diagnostic standpoint. A study of the X-ray films shows rather decidedly that the pulmonary processes in group 1 were more advanced and definitely active than in group 3. The discrepancies in the hospital group were no less. Further discrepancies were noted in the diagnosis of cavity formation. In 63 cases among the hospital group cavities were reported by the roentgenologist which gave no physical signs of such, and in 7 cases cavities were diagnosed clinically which failed to show in the roentgenogram. In only 11 cases of cavity did the two methods coincide. Likewise, there were discrepancies as to the gross location of the tuberculous process. This study brings out the fact that physical examination of the chest, done under good conditions and by experienced men, is rather uncertain by itself, and that the possibility of a pulmonary process, even quite extensive, cannot be ruled out because of negative physical findings. In fact, symptoms or history are really more helpful than the examination. Therefore, it seems reasonable that chest plates should be taken on all patients whose symptoms suggest tuberculosis, regardless of physical findings. Two cases in point are cited. It is true that there will be many negative reports. This cannot be helped. It should also be emphasized that negative roentgenograms are not conclusive evidence of the absence of tuberculosis, even in the lungs, as, in the hospital series referred to, 7 such cases, with positive clinical findings only, showed tubercle bacilli in the sputum. However, the positive X-ray findings will confirm and elaborate our knowledge of the pathology of the disease and reveal a not inconsiderable proportion of cases which would otherwise be missed. The ideal plan would be to take an X-ray of the chest at the first visit; the next best, to pay more attention to the patient's symptoms in selecting cases to be X-rayed. *Summary:* A series of patients was studied to determine the best criteria for requesting X-ray examinations of the chest in cases where the physical findings or symptoms suggest tuberculosis. The results tend to show that films should be taken whenever the symptoms suggest it and that the physical findings are less reliable guides.—*X-rays of the Chest: Their Use in Tuberculosis Suspects, R. T. Monroe and E. S. Emery, Jr., Boston, M. and S. J., April 8, 1926, cxciv, 619.*—(*A. P.*)

Limitations of X-ray Diagnosis of Pulmonary Tuberculosis.—The X-ray examination is indispensable in pulmonary tuberculosis, but its value is frequently exaggerated, and an unlimited significance cannot be attributed to it. It is only an adjunct to other methods, and permits the possibility of a diagnosis when correlated with all clinical findings. In the absence of clinical findings the roentgen picture alone is not sufficient. The foci must have a certain size and density to be determinable by the X-ray, and, therefore, a negative X-ray finding does not exclude the possibility of clinical tuberculosis. Fluoroscopy alone is not satisfactory; plates must be taken in addition. The plate is most important and can be elaborated upon by fluoroscopy. Deviations from normal without other findings cannot be considered pathological. Not all cavities can be determined roentgenlogically, and not all findings which appear to be cavities are really such.—*Fehlerquellen bei der Röntgenuntersuchung der Atmungsorgane, E. Peters, Beitr. z. Klin. d. Tuberk., 1924, lix, 375.*—(*H. J. C.*)

Technique of X-Ray Examination of Apices.—In general, the view of the apices in X-ray plates is obscured by the muscles and bones in these regions. If the patient sits or stands facing the tube, bends over by arching the spine, raises the chin, lowers the shoulders and crosses the arms over the abdomen, the clavicles are drawn caudalward; and the plate then taken shows the apices except the first interspace to be quite clear. Lateral motion of the chest helps to clear the first interspace. Such a procedure enables the röntgenographer to detect many small early lesions in the supraclavicular and infraclavicular regions.—*Zur Technik der Röntgendurchleuchtung und Aufnahme der Lungenspitzen, Gäbert, Klin. Wchnschr., November 18, 1924, iii, 2144.*—(*H. S. W.*)

Soft X-Ray Technique in Pulmonary Diagnosis.—A radiograph of a lung affected with tuberculosis may be made to show a very different picture, according to the quality of the rays employed. The hard ray will penetrate any early focus of tubercle and give an appearance similar to that of normal tissue. Old fibrotic foci, however, are opaque to the more penetrating and in fact to all rays. With hard-ray technique the negative of the normal chest shows little pulmonary detail; but with the soft ray there is seen scattered through both lungs a fine mottled and striated appearance, which represents the connective and interstitial tissue, the roots are much better defined, and their radiations plainly seen. The ribs appear as more or less indefinite shadows, and the fine bony markings in them are not evident. The details of the vertebral column are not seen, as the soft ray does not penetrate the heart and pericardium. (By soft rays is meant a secondary voltage of 45 kilovolts = an equivalent spark gap of about 4 inches = 4 benoist; by hard rays a secondary voltage of 60 to 70 kilovolts = an equivalent spark gap of about 6 inches = 6 to 7 benoist.) With soft-ray technique a recent pulmonary lesion in an early case, or a new focus in an old case, may be detected before physical signs have made their appearance. *Technique:* Duplitized films between two intensifying screens are used; distance between anticathode and film, 1 metre; secondary voltage, 45 kilovolts; milliamperage, 40; exposure 0.5 to 1 second, according to the thickness of the subject, the double focus Coolidge tube being employed. The technique should be so standardized and so recorded that it may be duplicated at subsequent sitting. The development of the film must also be standardized, the usual method being to develop for five minutes at 65°F.—*The Value of Soft Ray Technique in Pulmonary Radiography, B. Hudson, Lancet, October 17, 1925, ccix, 805.*—(*J. B. A.*)

Improved X-ray Technique in Chest Examination.—By varying posture and the position of the chest, shadows in the apices may be made much clearer although care must be taken not to allow the hilum shadow to be thrown too high or too much into the apical spaces.—*Zur Technik der verbesserten Lungenspitzendarstellung im Röntgenbilde, E. Meinicke, Deutsche med. Wchnschr., July 3, 1925, li, 1115.*—(*H. S. W.*)

Demonstration of Tubercle Bacilli in Suspected Material.—Material suspected of containing tubercle bacilli is inoculated into the guinea pig in the following manner: The animal is shaved on the right side and the material, to which has been added one drop of a 20 per cent dilution of sterile india ink, is inoculated intracutaneously in doses of 0.2 to 0.3 cc., and another larger dose is given subcutaneously on the left side. At about twelve or fourteen days after the inoculation, the skin at the site of inoculation is shaved, sterilized with iodine, and incised with sterile scalpel immediately over the point of inoculation, when, by pressure, the "core" of yellowish necrotic matter is expressed. Smears are made and stained for tubercle bacilli, and the expressed matter is then rubbed up for two to five minutes in a small drop of 10 to 20 per cent potassium solution, and the mixture is inoculated with

a capillary pipette into two tubes, each containing 40 cc. of Besredka's culture medium. Tubercle bacilli will grow in this medium very readily, and in from four to ten days after the inoculation of the medium, growth is evident, first as a cloud and later as a flaky granulation. The animal is kept for subsequent test with 0.1 cc. of a 20 per cent dilution of Old Tuberculin containing a trace of india ink. The report may be in the hands of the clinician within two weeks of the inoculation of the animal, and, a few days later than this, a good growth of the bacillus in question is on hand. The method is superior to Uhlenhuth's antiformin method because of the ease with which the diagnosis can be made even though there are but very few bacilli present.—*Zur Technik des beschleunigten Tuberkelbazillennachweises durch Tierversuch und Züchtung, E. Jacobsthal, Deutsche med. Wchnschr., January 22, 1926, lii, 144.*—(*H. S. W.*)

Alternating or Substituted Infections Masking Pulmonary Tuberculosis.—In 29 of 300 cases associated microörganisms in the sputa replaced the tubercle bacillus, the latter being found again after variable periods, and alternating with the substituted bacteria. The association plays a rôle in the disappearance of the bacillus because at this time the substituted bacteria may quickly dominate the field. These infections may be acute and fatal, or chronic and permanently displacing the tubercle bacillus. They may lead to error in diagnosis. Their prophylaxis and treatment is very important in itself.—*Des infections alternantes ou substitutées masquant la tuberculose pulmonaire, P. Courmont and Boissel, Meeting, Acad. de Médecine de Paris, May 19, 1925, reported in Presse Méd., May 16, 1925, no. 39, 647.*—(*E. H. K.*)

Cultivation of Tubercle Bacilli and Acid-Fast Saprophytes from Sputum.—To sputum was added an equal volume of 75 per cent glycerol and a small quantity of glucose, the latter's concentration not exceeding 5 per cent. The mixture was placed in the incubator at 37° for 24 hours, and, after removal of the glycerine by washing, the material was stained by the usual Ziehl-Neelsen method. It was possible to find tubercle bacilli in 9 of 27 cases examined, which were negative by the ordinary methods, and in 3 cases there were acid-fast saprophytes. These cases were all Turban-Gerhardt II. Tubercle bacilli were also found three times in 38 sputa from Turban I cases, and acid-fast saprophytes 10 times. In addition, acid-fast saprophytes were found in 10 of 45 healthy individuals.—*Vorversuche zur Züchtung der Tuberkelbacillen und säuerfesten Saprophyten im Auswurfe, J. Schiller, Centralbl. f. Bakt., 1925, xcvi, 92.*—(*H. J. C.*)

Sputum Staining Methods.—There is a relation between bacillary findings and the extent of pulmonary tuberculosis. An ideal method for the examination of tubercle bacilli does not exist. The Ziehl-Neelsen method, carefully used, is not inferior to any other methods. Less reliable is the Fränkel-Gabbet method. The Konrich method is highly recommended. It is questionable whether concentration methods are better than ordinary smear examinations. Cultivation and animal inoculation are indicated only in exceptional cases.—*Die klinische Bedeutung der Auswurfuntersuchung und ihre Vornahme in der Heilstätte, J. Fürbringer, Beitr. z. Klin. d. Tuberk., 1924, lix, 341.*—(*H. J. C.*)

Tubercle Bacilli in Feces.—The importance of obtaining definite evidence of tuberculosis, either by the examination of the sputum, if it can be obtained, or by other methods, if it cannot, is obvious. Many patients swallow a large portion of their sputum, and this is especially true of women and children. Hence, the necessity or the examination of the feces in many of these cases. The feces from 225 patients, including children not suffering from tuberculous disease, were examined for tubercle bacilli. The methods employed were (1) examination by direct smear or (2) some concentration method. The latter naturally gave more reliable results, and the ligroin method, modified from Lange and Nitsche, is recommended as being more rapid than the usual antiformin method. The slides, after staining with carbol-fuchsin, were decolorized in 25 per cent sulphuric acid for one hour, and then treated with absolute alcohol for fifteen minutes before being counterstained. Although it has been held that human feces contain nonpathogenic acid-fast bacilli derived particularly from milk and butter, it is believed that no bacillus other than the tubercle bacillus would retain the carbol-fuchsin stain after such intensive decolorization as mentioned above. Furthermore, children on a similar diet but not clinically tuberculous never showed acid-fast bacilli in the feces. In all cases which showed tubercle bacilli to be consistently present in the sputum, acid-fast bacilli were demonstrable in the feces, and in no case in which the sputum result was negative on repeated examination could acid-fast bacilli be found in the feces. There is little doubt that the acid-fast bacilli

found in the feces of children suffering from pulmonary tuberculosis are tubercle bacilli derived largely from swallowed sputum. The possibility that some bacilli may originate from tuberculous ulceration of the intestine must be considered, although this is apparently not frequently their source. Of 85 positive cases, 61 gave both positive sputum and feces, and 24 positive feces only. In the majority of these patients the symptoms and physical signs were sufficiently marked as to leave little doubt as to the diagnosis, but the advantage of obtaining definite confirmatory evidence, when no sputum is available, in such a high proportion of cases (24 out of 85) is sufficiently obvious. When the clinical signs were not so definite 70 cases showed tubercle bacilli in the sputum at one time or another, a percentage of 38.6, while 85 showed tubercle bacilli in the feces, a percentage of 46.9. A method which increases the certainty of diagnosis by at least 9 per cent is worthy of an extended trial, especially with regard to children.—*Tubercle Bacilli in Faeces. A Note on the Examination of the Faeces of 225 Tuberculous Children, K. A. H. Sykes, Lancet, February 6, 1926, ccx, 273.—(J. S. W.)*

Diagnostic Value of Lipiodol.—As fundamental bases for interpretation of X-rays after lipiodol injection the following points should be emphasized: *1:* This substance makes opaque only a very small part of the bronchial tree, since 40 cc. are injected and the normal lung volume is five litres. Too large an amount causes a confused picture, while the small amount may not penetrate the desired area. *2:* The liquid makes its way to the bronchial terminations by two forces, weight and thoracic aspiration. It is therefore best to have the patient inspire deeply during the injection, and to allow free movement of the side of the thorax to be examined. The lipiodol may meet with certain obstacles, such as stenosis or compression of a large bronchus, or stenosis of the bronchus of drainage of a cavity, abundant pathological secretions, and insufficient thoracic aspiration, as in emphysema, immobilization from scar-tissue, pleural adhesions, or diaphragmatic paralysis. While the bronchial tree cannot be explored with the same thoroughness as the digestive tract or the ureter and renal pelvis, the following conclusions may be drawn: *1:* A positive image, presenting exact morphological characters, has an absolute diagnostic value. *2:* A negative image has only a relative value, and must be interpreted with caution, since the lipiodol may not have reached the diseased portion. A delayed positive image may sometimes be obtained in such instances, particularly in emphysematous chests, by taking another X-ray after a couple of days. Characteristic shadows may be cast by a cavity with its bronchus of drainage, various types of bronchial dilatation, or peribronchial abscess, deviation of the trachea, and fistulous tracts, and their interpretation is not difficult. But doubtful images of difficult interpretation are frequent, and may be of the pigeon's nest type, signifying possibly but not surely a dilated bronchus, or the cylindrical type, appearing like a dilated bronchus but really a normal one appearing unduly large because in an anterior view it is near the surface, or sharply terminated bronchial shadows as seen in emphysema. *General conclusions: 1:* This method may give definitely positive findings. *2:* It may assist in the differential diagnosis between bronchopulmonary or pleural suppurations. *3:* It leaves room for uncertainty in negative or doubtful images. *4:* It may lead to error by erroneous interpretation.—*Ce que la clinique peut demander aux injections intratrachéales de lipiodol dans le radiodiagnostic des affections de l'appareil respiratoire; difficultés et erreurs d'interprétation, E. Sergent and P. Cottenot, Presse Méd., April 18, 1925, no. 31, 500.—(E. H. K.)*

Lipiodol for Topographical Diagnosis of Pneumothorax.—Injections of lipiodol into the pleural cavity have furnished precise information which could not be obtained by radioscopy or radiography. It is especially useful in cases of artificial pneumothorax complicated by exudate. In such cases Jacobaeus has practised fluoroscopy with the head lowered, which is, however, fatiguing and uncomfortable for the patient and not entirely satisfactory for the observer. In the case of large effusions, no manoeuvres will reveal the limits of the pleural cavity. Lipiodol injected in small quantities (2 or 3 cc.) will, however, furnish exact information. Injected slowly under the fluoroscope it may be seen to descend slowly in drops to reach the bottom of the pleura. The patient is then turned, first on one side, then on the other, and the lateral limits determined. It is well tolerated. In one case observed, the existence of quite a large pleural adhesion could be diagnosed by the arrest of a portion of the opaque liquid, as though suspended. It was also attempted to find the site of a pleurobronchial fistula in a patient who was coughing up pleural pus, but this was not successful, probably because the orifice of the fistula was situated where the lipiodol failed to come in contact with it.—*Emploi du lipiodol pour determiner les limites de la cavité pleurale dans les pnéumothorax, J.*

Genêvrier, Meeting, Section d'études scientifiques de l'Oeuvre de la Tuberculose, March 14, 1925, reported in Rev. d. l. Tuberc., June, 1925, vi, 396.—(A. P.)

Intratracheal Injections of Lipiodol.—The literature on the use of lipiodol, in the diagnosis first of spinal cord tumors and later of bronchiectasis and lung abscess, is reviewed. For the latter purpose a small curved trocar and cannula are introduced through the cricothyroid membrane under local anesthesia and about 5 cc. of 1 per cent novocaine injected into the trachea. This is followed by 15 to 20 cc. of warm lipiodol with the patient in such a position that the oil will flow into the involved area. Roentgenograms are made at once. The greater part of the lipiodol is removed by coughing within a few hours after the injection. No immediate or late ill effects have been observed. It is pointed out that the location and extent of the involved areas in bronchiectasis and chronic lung abscess can be more accurately determined by this method, which is a matter of some importance to the thoracic surgeon. A number of roentgenograms illustrating these conditions in a short series of cases are included in the article.—*Demonstration of the Bronchial Tree by Intratracheal Injections of Lipiodol, H. W. Grady, Am. J. Roentgenol. & Rad. Ther., January, 1926, xv, 65.—(E. H. K.)*

Lipiodol in Pulmonary Diagnosis.—Insufflation of a contrast medium (lipiodol) by normal persons will sometimes produce misleading results if the material gets into the alveoli, for in such circumstances the shadows may resemble infiltration or saccular bronchiectasis. The fluoroscopic picture is better than the plate for interpreting the results. The lipiodol which reaches the alveoli may remain for months, while that in the bronchi is coughed up in a few hours.—*Röntgenuntersuchungen an normalen und kranken Bronchien nach Füllung mit Lipiodol, R. Lenk and F. Haslinger, Klin. Wchnschr., August 6, 1925, iv, 1533.—(H. S. W.)*

Oils in X-Ray Diagnosis of Bronchiectasis.—The use of a contrasting oil (iodine and sesamoil) intratracheally gives a very satisfactory differentiation in bronchiectasis, although when the oil fills cavities the picture is not as clear as it is when dilated bronchi only contain the oil.—*Die Röntgendiagnose der Bronchiektasie mittels Kontrastöl, W. Landau, Deutsche med. Wchnschr., July 3, 1925, li, 1115.—(H. S. W.)*

Different Tuberculin Diagnostic Methods.—The percutaneous (Moro) reaction is positive in 80 to 90 per cent of cases. When this is negative 0.1 mgm. of tuberculin may be injected subcutaneously and, if no reaction follows this, 1 mgm. may be given subcutaneously on the next day. If no reaction follows these tests during the next three days, the patient is considered to be tuberculosis-free. If doubtful, the entire series may be repeated in one week. A table comparing the relative sensitiveness of the Moro and the Pirquet reactions shows the Moro to have a considerably higher percentage of positives than the Pirquet.—*Ueber die Brauchbarkeit verschiedener Tuberkulinisierungsmethoden zu diagnostischen Zwecken, H. Czickli and R. Haller, Wien. klin. Wchnschr., January 29, 1925, xxxviii, 138.—(H. S. W.)*

Tuberculin Skin Reactions.—Old Tuberculin, bovine tuberculin and Ponndorf tuberculin A and B were compared in 150 cases. The Petruschky modified method was used. There was found no difference in reaction following inunction or merely allowing the dry tuberculin to act. In comparing the various tuberculins the bovine exceeded O. T. by 67 per cent. Ponndorf B cannot be used as a purely diagnostic agent. In differential diagnosis a positive bovine reaction is to be viewed cautiously. Prognostically, the cutaneous reaction is very limited, and is to be used only in combination with clinical findings. It gives no information regarding the grade of activity, and is inferior to temperature and weight determinations. When very active preparations for cutaneous application are desired, Ponndorf's tuberculins are to be recommended.—*Spezifische Cutanreaktionen, P. Hornung, Beitr. z. Klin. d. Tuberk., 1924, lix, 74.—(H. J. C.)*

Tuberculin Skin Reactions in Adult.—This reaction, of such diagnostic importance in infancy, is generally regarded as of no value in the adult, because of the frequency of latent tuberculosis. The reason for the discredit into which the reaction has fallen in the adult seems to depend on the fact that generally note is taken only of whether it is positive or negative, and its quantitative and qualitative variations ignored. Of particular interest is the earliness at which the reaction appears. Some cases show such a marked and intense reaction as almost to constitute a local disease like erysipelas. In order to note the earliness of appearance of the reaction it is advisable to make the test in the morning. Three factors should be noted: (1) precocity of appearance, (2) intensity, and (3) duration. There are three principal modalities the reaction may

assume: *1:* A delayed and feeble reaction, with perhaps slight infiltration persisting not over two or three days, leaving a slight reddish spot: *2:* A reaction appearing in about twenty-four hours, attaining its maximum in about forty-eight hours, with more marked and persistent infiltration. *3:* An early reaction, with infiltration manifest in five or six hours, attaining its maximum at twenty-four hours, very intense, often vesicular or necrotic, and subsiding only slowly. *Cutireaction in clinically nontuberculous persons:* There were 200 such cases, of which 156 showed a positive reaction (78 per cent), but almost always of slight degree (type 1). *Cutireaction in tuberculous individuals:* Except in the cachectic cases, the reaction was generally much stronger, and appeared much earlier and lasted longer. In early discrete and fibroid types in good condition, an early and intense reaction was the rule, less so in the chronic progressive or active cases, and weak or absent in those in poor condition or manifesting acute exacerbations. An early and intense reaction, generally speaking, means a favorable prognosis. *Cultireaction in patients with serofibrinous pleurisy:* There were 50 cases. The striking features of the reaction were its precocity, intensity, and long duration. As early as the third hour a slight erythema was noticeable, and beginning infiltration; by the fifth hour there was a definite nodule with a red halo. The reaction might persist at its height for five or six days. Even at the moment of scarification a small red halo was common, followed by blanching, the *témoin à la tuberculine.* These characteristics hold only for so called primary tuberculous pleurisies. *Interpretation:* In an individual presenting no clinical signs of tuberculosis the presence of an early intense reaction favors the probability of the disease, while in one already affected it generally signifies a favorable prognosis. It is possible, however, for a good general condition to coexist with active disease, in which case it may be misleading. Generally, however, coincident with a serious exacerbation, the reaction diminishes. Serial observations are of more value than the single ones.—*Les diverses modalités de la cutiréaction à la tuberculine chez l'adulte, F. Benzançon and A. Vigneron, Meeting, Section d'études scientifiques de l'Oeuvre de la tuberculose, March 14, 1925, reported in Rev. d. l. Tuberc., June, 1925, vi, 363.*—(*A. P.*)

Time Factors of Tuberculin Reaction.—The febrile reaction following a tuberculin injection is definite for one and the same individual, and is independent of whether the tuberculin was administered by the intracutaneous, subcutaneous or intravenous route. The relation between the duration and height of the fever is always the same in the same individual, as is also the time from the moment of injection to the height of the temperature curve, regardless of the dose injected. The explanation of this fact is to be found in the anatomic nature of the tuberculous focus. Active, progressive processes give a short, and inactive benign processes a longer reaction time. The less dense the surrounding fibrous tissue and the more active the process, the more rapidly does the reaction develop.—*Studien zum Tuberkulinproblem. VI. Mitt. Über die Reaktionszeit der Tuberkulinreaktion. (Ein Beitrag zur Frage der spezifischen Wirkung des Tuberkulins.) A. V. v. Frisch, Beitr. z. Klin. d. Tuberk., 1924, lx, 155.*—(*H. J. C.*)

Reaction of Eosinophiles to Tuberculin in Diagnosis of Pulmonary Tuberculosis.—The behavior of the eosinophile may be of value in the diagnosis of active pulmonary tuberculosis. Two phases occur, the first a more or less outspoken drop in the eosinophile count and the second an increase in count. The latter phase is especially valuable for the prognosis of pulmonary tuberculosis while the first, even though found by Zappert to possess no especial significance, was utilized practically by injecting small amounts of tuberculin, which in active tuberculosis caused a drop in eosinophiles, while in the healthy nonallergic organism these small amounts produced no changes. It is believed that this drop in the eosinophiles is a valuable sign in the early diagnosis of active pulmonary tuberculosis. The method is simple and consists of determining the absolute count of eosinophiles in a cubic millimetre of blood, then injecting 0.000,000,001 cc. of bouillon filtrate, and a half-hour later again counting the eosinophiles, when a drop in the count indicates a diagnosis of active tuberculosis.—*Ein neuer Versuch spezifischer Diagnostik aktiver Formen initialer Lungentuberkulose, F. A. Michailow, Virchow's Arch. f. path. Anat., 1925, cclvi, 620.*—(*H. J. C.*)

Specificity of Tuberculin Reaction Questioned.—As time goes on, there develops more opposition to the idea of the specificity of the tuberculin skin reaction. Foreign bodies and irritating substances produce a reaction that can hardly be differentiated from the tuberculin reaction, and the tuberculin reaction, anatomically and biologically cannot be regarded as a newly formed tuberculous focus. A similar

structure, even though of less violent reaction, can be caused by colon bacilli. Even the inflammatory reaction is not specific, so that its value in diagnosis and prognosis may be questioned. The present investigations were made on 9 tuberculous patients (3 cases of lupus and 6 of pulmonary tuberculosis) and 15 healthy persons. Intracutaneous injections were made with tubercle-bacillus and colon-bacillus preparations. Both produced reactions, as well as the flaring-up of old foci, once with a general reaction. The tubercle-bacillus and colon-bacillus areas of reaction were excised in 6 tuberculous individuals. Histologically, the differences were only quantitative. The local reactions were also excised in 9 clinically healthy persons. The findings did not differ greatly from those in the tuberculous.—*Zur Spezifität der Tuberkulinreaktion mit besonderer Berücksichtigung ihres histologischen Charakters, W. Blumenberg, Beitr. z. Klin. d. Tuberk., 1925, lxi, 509.*—(*H. J. C.*)

Effect of Tuberculin on Complement Fixation.—In a series of tuberculous patients small doses of tuberculin caused an increase of complement-binding bodies if coincident focal and general reactions occurred. The increase also occurred after repeated tuberculin administration without visible reaction. In non-tuberculous persons repeated large tuberculin doses changed a negative to a positive complement-fixation reaction.—*Antikörperbildung nach Tuberkulinisierung, T. Gruschka and E. Guth, Ztschr. f. Tuberk., 1925, xliii, 103.*—(*H. J. C.*)

Complement Fixation in Tuberculosis.—In order to evaluate clinically the Wassermann and Besredka methods, 100 cases were examined, to correlate these with activity or inactivity and with the sedimentation rate, the specific skin reaction and the behavior of the leucocytes. These two methods are of only indefinite value in the differentiation of activity from inactivity. In outspoken positive Besredka complement-fixation tests 84.37 per cent were definitely tuberculosis, while with the Wassermann reaction these were 62.5 per cent. In cases with slight symptoms the Besredka reaction was positive in 60 per cent and the Wassermann in 45 per cent, indicating that the Besredka reaction is the more reliable of the two in practice. In cases in which the sedimentation reaction and leucocytes indicate tuberculosis, a positive complement-fixation reaction is significant. A positive complement fixation coincident with a lymphocytosis, even in the absence of clinical symptoms, indicates activity. Blood cell picture is verified. Leucocytosis, neutrophilia and a shift to the left were found in extensive processes of unfavorable prognosis; lymphocytosis, on the other hand, was noted in early cases and older processes with favorable prognosis. Eosinophilia and an increase of eosinophiles after a preliminary decrease are favorable prognostically.—*Die klinische Beurteilung der Komplementablenkung nach Wassermann und Besredka unter Berücksichtigung der spezifischen Hautreaktion, Blutkörperchensenkungsreaktion und des weissen Blutbildes, F. Scheidemandel, Ztschr. f. Tuberk., 1925, xlii, 363.*—(*H. J. C.*)

Red Cell Sedimentation Reaction.—The sedimentation time is valuable in the determination of temporary activity and the anatomical character of the tuberculous process. The lower normal value in healthy men is 5, and in healthy women 4. Questionable cases, however, occur, in which a definite active pulmonary tuberculosis exists but the sedimentation rate is normal.—*Blutkörperchensenkung und aktive Lungentuberkulose, A. Freund, Beitr. z. Klin. d. Tuberk., 1924, lix, 629.*—(*H. J. C.*)

Key to Abstractors

A. P.: Andrew Peters, Loomis, N. Y.
E. H. K.: E. H. Kerper, Loomis, N. Y.
E. R. L.: Esmond R. Long, Chicago, Ill.
H. J. C.: H. J. Corper, Denver, Col.
H. S. W.: H. S. Willis, Baltimore, Md.
J. B. A.: J. Burns Amberson, Detroit, Mich.
J. C. D.: J. C. Dundee, Loomis, N. Y.
J. S. W.: J. Stanley Woolley, Loomis, N. Y.